

I 3

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶: G01N 33/53	A2	(11) International Publication Number: WO 98/45704 (43) International Publication Date: 15 October 1998 (15.10.98)
(21) International Application Number: PCT/DK98/00145 (22) International Filing Date: 7 April 1998 (07.04.98) (30) Priority Data: 0392/97 7 April 1997 (07.04.97) DK (71) Applicant (for all designated States except US): NOVO NORDISK A/S [DK/DK]; Novo Allé, DK-2880 Bagsvaerd (DK). (72) Inventors; and (75) Inventors/Applicants (for US only): THASTRUP, Ole [DK/DK]; Birkevej 37, DK-3460 Birkerød (DK). PETERSEN BJØRN, Sara [DK/DK]; Klampenborgvej 102, DK-2800 Lyngby (DK). TULLIN, Søren [DK/DK]; Karl Gjellerups Alle 18, DK-2860 Søborg (DK). KASPER, Almholt [DK/DK]; Eigilsgade 32, 4. tv, DK-2300 København S (DK). SCUDDER, Kurt [US/DK]; Lavendelhaven 70, DK-2830 Virum (DK). (74) Common Representative: NOVO NORDISK A/S; attn. Lars Kellberg, Novo Allé, DK-2880 Bagsvaerd (DK).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: A METHOD FOR EXTRACTING QUANTITATIVE INFORMATION RELATING TO AN INFLUENCE ON A CELLULAR RESPONSE		
(57) Abstract <p>Cells are genetically modified to express a luminophore, e.g., a modified (F64L, S65T, Y66H) Green Fluorescent Protein (GFP, EGFP) coupled to a component of an intracellular signalling pathway such as a transcription factor, a cGMP- or cAMP-dependent protein kinase, a cyclin-, calmodulin- or phospholipid-dependent or mitogen-activated serine/threonine protein kinase, a tyrosine protein kinase, or a protein phosphatase (e.g. PKA, PKC, Erk, Smad, VASP, actin, p38, Jnk1, PKG, IkappaB, CDK2, Grk5, Zap70, p85, protein-tyrosine phosphatase 1C, Stat5, NFAT, NFkappaB, RhoA, PKB). An influence modulates the intracellular signalling pathway in such a way that the luminophore is being redistributed or translocated with the component in living cells in a manner experimentally determined to be correlated to the degree of the influence. Measurement of redistribution is performed by recording of light intensity, fluorescence lifetime, polarization, wavelength shift, resonance energy transfer, or other properties by an apparatus consisting of e.g. a fluorescence microscope and a CCD camera. Data stored as digital images are processed to numbers representing the degree of redistribution. The method can be used as a screening program for identifying a compound that modulates a component and is capable of treating a disease related to the function of the component.</p>		

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi		
CA	Canada	IT	Italy				
CH	Switzerland						
CY	Cyprus						
DE	Germany						
DK	Denmark						
EE	Estonia						
EG	Egypt						
ES	Spain						
ET	Ethiopia						
FI	Finland						
FR	France						
GA	Gabon						
GB	United Kingdom						
GE	Georgia						
GH	Ghana						
GN	Guinea						
GR	Greece						
HU	Hungary						
IE	Ireland						
IL	Israel						
IS	Iceland						
IT	Italy						
JM	Jamaica						
KR	Republic of Korea						
KZ	Kazakhstan						
LC	Saint Lucia						
LI	Liechtenstein						
LK	Sri Lanka						
LU	Luxembourg						
LV	Latvia						
LY	Libya						
MA	Morocco						
MC	Monaco						
MD	Republic of Moldova						
ME	Montenegro						
MG	Madagascar						
MH	Marshall Islands						
MI	Maldives						
MK	The former Yugoslav Republic of Macedonia						
ML	Mali						
MN	Mongolia						
MO	Macao						
MP	Northern Mariana Islands						
MQ	Martinique						
MR	Mauritania						
MT	Malta						
MU	Mauritius						
MV	Maldives						
MW	Malawi						
MX	Mexico						
MY	Malaysia						
MZ	Mozambique						
NA	Namibia						
NC	New Caledonia						
NE	Niger						
NG	Nigeria						
NL	Netherlands						
NO	Norway						
NP	Nepal						
NR	Norfolk Island						
NU	Niue						
PB	Puerto Rico						
PE	Peru						
PF	French Polynesia						
PG	Papua New Guinea						
PH	Philippines						
PK	Pakistan						
PL	Poland						
PM	St. Pierre and Miquelon						
PN	Pitcairn Islands						
PT	Portugal						
RO	Romania						
RU	Russian Federation						
SD	Sudan						
SE	Sweden						
SG	Singapore						
SH	St. Helena						
SI	Slovenia						
SJ	Svalbard and Jan Mayen						
SK	Slovakia						
SL	Sierra Leone						
SM	San Marino						

A METHOD for extracting quantitative information relating to an influence on a cellular response

FIELD OF INVENTION

5 The present invention relates to a method and tools for extracting quantitative information relating to an influence, on a cellular response, in particular an influence caused by contacting or incubating the cell with a substance influencing a cellular response, where the cellular response is manifested in redistribution of at least one component in the cell. In particular, the invention relates to a method for extracting quantitative information relating to an influence on an intracellular pathway involving redistribution of at least one component associated with the pathway. The method of the invention may be used as a very efficient procedure for testing or discovering the influence of a substance on a physiological process, for example in connection with screening for new drugs, testing of substances for toxicity, identifying drug targets for known or novel drugs. Other valuable uses of the method and technology of the invention will be apparent to the skilled person on the basis of the following disclosure. In a particular embodiment of the invention, the present invention relates to a method of detecting intracellular translocation or redistribution of biologically active polypeptides, preferably an enzyme, affecting intracellular processes, and a DNA construct and a cell for use in the method.

20

BACKGROUND OF THE INVENTION

Intracellular pathways are tightly regulated by a cascade of components that undergo modulation in a temporally and spatially characteristic manner. Several disease states can be attributed to altered activity of individual signalling components (i.e. protein kinases, protein phosphatases, transcription factors). These components therefore render themselves as attractive targets for therapeutic intervention.

25 Protein kinases and phosphatases are well described components of cellular signalling pathways. They are involved in a wide range of cellular processes, including cell growth, differentiation, and cell death. Although the involvement of protein kinases in cellular signalling and regulation have been subjected to extensive studies, detailed knowledge on e.g. the exact timing and spatial characteristics of signalling events is often difficult to obtain due to lack of a convenient technology.

Novel ways of monitoring specific modulation of intracellular pathways in intact, living cells is assumed to provide new opportunities in drug discovery, functional genomics, toxicology, patient monitoring etc.

5 The spatial orchestration of protein kinase activity is likely to be essential for the high degree of specificity of individual protein kinases. The phosphorylation mediated by protein kinases is balanced by phosphatase activity. Also within the family of phosphatases translocation has been observed, e.g. translocation of PTP2C to membrane ruffles [(Cossette *et al.* 1996)], and likewise is likely to be indicative of phosphatase activity.

Protein kinases often show a specific intracellular distribution before, during and after activation. Monitoring the translocation processes and/or redistribution of individual protein kinases or subunits thereof is thus likely to be indicative of their functional activity. A connection between translocation and catalytic activation has been shown for protein kinases like the diacyl glycerol (DAG)-dependent protein kinase C (PKC), the cAMP-dependent protein kinase (PKA) [(DeBernardi *et al.* 1996)] and the mitogen-activated-protein kinase Erk-1 [(Sano *et al.* 1995)].

Commonly used methods of detection of intracellular localisation/activity of protein kinases and phosphatases are immunoprecipitation, Western blotting and immunocytochemical detection.

20 Taking the family of diacyl glycerol (DAG)-dependent protein kinase Cs (PKCs) as an example, it has been shown that individual PKC isoforms that are distributed among different tissues and cells have different activator requirements and undergo differential translocation in response to activation. Catalytically inactive DAG-dependent PKCs are generally distributed throughout the cytoplasm, whereas they upon activation translocate to become associated with different cellular components, e.g. plasma membrane [(Farese, 1992), (Fulop Jr. *et al.* 1995)] nucleus [(Khalil *et al.* 1992)], cytoskeleton [(Blobe *et al.* 1996)]. The translocation phenomenon being indicative of PKC activation has been monitored using different approaches: a) immunocytochemistry where the localisation of individual isoforms can be detected after permeabilisation and fixation of the cells [(Khalil *et al.* 1992), (Fulop Jr. *et al.* 1995)], b) monitoring of the translocation of fluorescently labelled PKCs, e.g. with the fluorophore PKC α [(Bastiaens *et al.* 1996)] and c) genetic tagging of PKC α [(Schnidt *et al.* 1997)] and of PKC γ and PKC ϵ [(Sakai *et al.* 1996)]. The first method does not provide dynamic information whereas the latter methods will. Tagging PKC with fluorescently labelled photolabile protecting groups

distinguish between different DAG-dependent isoforms of PKC but will label and show movement of all isoforms. Chemical and genetic labelling of specific DAG-dependent PKCs confirmed that they in an isoform specific manner upon activation move to cell periphery or nucleus.

- 5 In an alternative method, protein kinase A activity has been measured in living cells by chemical labelling one of the kinase's subunit (Adams *et al.* 1991). The basis of the methodology is that the regulatory and catalytic subunit of purified protein kinase A is labelled with fluorescein and rhodamine, respectively. At low cAMP levels protein kinase A is assembled in a heterotetrameric form which enables fluorescence resonance energy transfer between
10 the two fluorescent dyes. Activation of protein kinase A leads to dissociation of the complex, thereby eliminating the energy transfer. A disadvantage of this technology is that the labelled protein kinase A has to be microinjected into the cells of interest. This highly invasive technique is cumbersome and not applicable to large scale screening of biologically active substances. A further disadvantage of this technique as compared to the presented invention is
15 that the labelled protein kinase A cannot be inserted into organisms/animals as a transgene.

- Recently it was discovered that Green Fluorescent Protein (GFP) expressed in many different cell types, including mammalian cells, became highly fluorescent [(Chalfie *et al.* 1994)]. WO95/07463 describes a cell capable of expressing GFP and a method for detecting a protein of interest in a cell based on introducing into a cell a DNA molecule having DNA sequence encoding the protein of interest linked to DNA sequence encoding a GFP such that
20 the protein produced by the DNA molecule will have the protein of interest fused to the GFP, then culturing the cells in conditions permitting expression of the fused protein and detecting the location of the fluorescence in the cell, thereby localizing the protein of interest in the cell. However, examples of such fused proteins are not provided, and the use of fusion proteins with GFP for detection or quantitation of translocation or redistribution of biologically
25 active polypeptides affecting intracellular processes upon activation, such as proteins involved in signalling pathways, e.g. protein kinases or phosphatases, has not been suggested. WO 95/07463 further describes cells useful for the detection of molecules, such as hormones or heavy metals, in a biological sample.

WO 95/07463 further describes a cell which contains a regulatory element which in turn will affect the expression of the GFP. In this way the gene encoding GFP is used as a reporter gene in a cell which is constructed for monitoring the presence of a specific molecular identity.

Green Fluorescent Protein has been used in an assay for the detection of translocation of the glucocorticoid receptor (GR) [Carey, KL et al., The Journal of Cell Biology, Vol. 133, No. 5, p. 985-996 (1996)]. A GR-S65TGFP fusion has been used to study the mechanisms involved in translocation of the glucocorticoid receptor (GR) in response to the agonist dexamethasone from the cytosol, where it is present in the absence of a ligand, through the nuclear pore to the nucleus where it remains after ligand binding. The use of a GR-GFP fusion enables real-time imaging and quantitation of nuclear/cytoplasmic ratios of the fluorescence signal.

Many currently used screening programmes designed to find compounds that affect protein kinase activity are based on measurements of kinase phosphorylation of artificial or natural substrates, receptor binding and/or reporter gene expression.

DISCLOSURE OF THE INVENTION

The present invention provides an important new dimension in the investigation of cellular systems involving redistribution in that the invention provides quantification of the redistribution responses or events caused by an influence, typically contact with a chemical substance or mixture of chemical substances, but also changes in the physical environment. The quantification makes it possible to set up meaningful relationships, expressed numerically, or as curves or graphs, between the influences (or the degree of influences) on cellular systems and the redistribution response. This is highly advantageous because, as has been found, the quantification can be achieved in both a fast and reproducible manner, and - what is perhaps even more important - the systems which become quantifiable utilizing the method of the invention are systems from which enormous amounts of new information and insight can be derived.

The present screening assays have the distinct advantage over other screening assays, e.g., receptor binding assays, enzymatic assays, and reporter gene assays, in providing a system in which biologically active substances with completely novel modes of action, e.g. inhibition or promotion of receptor binding,

can be studied in a way that insures very high selectivity to the particular isoform of the biologically active polypeptide and further development of compound selectivity versus other isoforms of

the same biologically active polypeptide or other components of the same signalling pathway.

In its broadest aspect, the invention relates to a method for extracting quantitative information relating to an influence on a cellular response, the method comprising recording variation, caused by the influence on a mechanically intact living cell or mechanically intact living cells, in spatially distributed light emitted from a luminophore, the luminophore being present in the cell or cells and being capable of being redistributed in a manner which is related with the degree of the influence, and/or of being modulated by a component which is capable of being redistributed in a manner which is related to the degree of the influence, the association resulting in a modulation of the luminescence characteristics of the luminophore, detecting and recording the spatially distributed light from the luminophore, and processing the recorded variation in the spatially distributed light to provide quantitative information correlating the spatial distribution or change in the spatial distribution to the degree of the influence. In a preferred embodiment of the invention the luminophore, which is present in the cell or cells, is capable of being redistributed by modulation of an intracellular pathway, in a manner which is related to the redistribution of at least one component of the intracellular pathway. In another preferred embodiment of the invention, the luminophore is a fluorophore.

The cells

In the invention the cell and/or cells are mechanically intact and alive throughout the experiment. In another embodiment of the invention, the cell or cells is/are fixed at a point in time after the application of the influence at which the response has been predetermined to be significant, and the recording is made at an arbitrary later time.

The mechanically intact living cell or cells could be selected from the group consisting of fungal cell or cells, such as a yeast cell or cells; invertebrate cell or cells including insect cell or cells; and vertebrate cell or cells, such as mammalian cell or cells. This cell or these cells is/are incubated at a temperature of 30°C or above, preferably at a temperature of from 32°C to 39°C, more preferably at a temperature of from 35°C

The mechanically intact living cell or cells could be a part of a matrix of identical or non-identical cells.

A cell used in the present invention should contain a nucleic acid construct encoding a fusion polypeptide as defined herein and be capable of expressing the sequence encoded by the construct. The cell is a eukaryotic cell selected from the group consisting of fungal cells, such as yeast cells; invertebrate cells including insect cells; vertebrate cells such as mam-
5 malian cells. The preferred cells are mammalian cells.

In another aspect of the invention the cells could be from an organism carrying in at least one of its component cells a nucleic acid sequence encoding a fusion polypeptide as defined herein and be capable of expressing said nucleic acid sequence. The organism is selected from the group consisting of unicellular and multicellular organisms, such as a mammal.
10

The luminophore

The luminophore is the component which allows the redistribution to be visualised and/or recorded by emitting light in a spatial distribution related to the degree of influence. In one embodiment of the invention, the luminophore is capable of being redistributed in a manner
15 which is physiologically relevant to the degree of the influence. In another embodiment, the luminophore is capable of associating with a component which is capable of being redistributed in a manner which is physiologically relevant to the degree of the influence. In another embodiment, the luminophore correlation between the redistribution of the luminophore and the degree of the influence could be determined experimentally. In a preferred aspect of the
20 invention, the luminophore is capable of being redistributed in substantially the same manner as the at least one component of an intracellular pathway. In yet another embodiment of the invention, the luminophore is capable of being quenched upon spatial association with a component which is redistributed by modulation of the pathway, the quenching being measured as a change in the intensity of the luminescence.

25 The luminophore could be a fluorophore. In a preferred embodiment of the invention, the luminophore could be a polypeptide encoded by and expressed from a nucleotide sequence harboured in the cell or cells. The luminophore could be a hybrid polypeptide comprising a fusion of at least a portion of each of two polypeptides.

The luminescent polypeptide could be a GFP as defined herein or could be selected from the group consisting of green fluorescent proteins having the F64L mutation as defined herein.

such as F64L-GFP, F64L-Y66H-GFP, F64L-S65T-GFP, and EGFP. The GFP could be N- or C-terminally tagged, optionally via a peptide linker, to the biologically active polypeptide or a part or a subunit thereof. The fluorescent probe could be a component of an intracellular signalling pathway. The probe is coded for by a nucleic acid construct.

- 5 The pathway of investigation in the present invention could be an intracellular signalling pathway.

The influence

- 10 In a preferred embodiment of the invention, the influence could be contact between the mechanically intact living cell or the group of mechanically intact living cells with a chemical substance and/or incubation of the mechanically intact living cell or the group of mechanically intact living cells with a chemical substance. The influence will modulate the intracellular processes. In one aspect the modulation could be an activation of the intracellular processes. In another aspect the modulation could be an deactivation of the intracellular processes.
- 15 In yet another aspect, the influence could inhibit or promote the redistribution without directly affecting the metabolic activity of the component of the intracellular processes.

In one embodiment the invention is used as a basis for a screening program, where the effect of unknown influences such as a compound library, can be compared to influence of known reference compounds under standardised conditions.

20

The recording

- In addition to the intensity, there are several parameters of fluorescence or luminescence which can be modulated by the effect of the influence on the underlying cellular phenomena, and can therefore be used in the invention. Some examples are resonance energy transfer,
- 25 fluorescence lifetime, polarisation, wavelength shift. Each of these methods requires a particular kind of filter in the emission light path to select the component of the light desired and reject other components. The recording of the

- 30 In one embodiment of the invention, the spatially distributed light emitted by a luminophore could be detected by a change in the resonance energy transfer between the luminophore and another luminescent entity capable of delivering energy to the luminophore. Each of

which has been selected or engineered to become part of, bound to or associated with particular components of the intracellular pathway. In this embodiment, either the luminophore or the luminescent entity capable of delivering energy to the luminophore undergoes redistribution in response to an influence. The resonance energy transfer would be measured as a
5 change in the intensity of emission from the luminophore, preferably sensed by a single channel photodetector which responds only to the average intensity of the luminophore in a non-spatially resolved fashion.

In one embodiment of the invention, the recording of the spatially distributed light could be made at a single point in time after the application of the influence. In another embodiment,
10 the recording could be made at two points in time, one point being before, and the other point being after the application of the influence. The result or variation is determined from the change in fluorescence compared to the fluorescence measured prior to the influence or modulation. In another embodiment of the invention, the recording could be performed at a series of points in time, in which the application of the influence occurs at some time after
15 the first time point in the series of recordings, the recording being performed, e.g., with a predetermined time spacing of from 0.1 seconds to 1 hour, preferably from 1 to 60 seconds, more preferably from 1 to 30 seconds, in particular from 1 to 10 seconds, over a time span of from 1 second to 12 hours, such as from 10 seconds to 12 hours, e.g., from 10 seconds to one hour, such as from 60 seconds to 30 minutes or 20 minutes. The result or variation is
20 determined from the change in fluorescence over time. The result or variation could also be determined as a change in the spatial distribution of the fluorescence over time.

Apparatus

The recording of spatially distributed luminescence emitted from the luminophore is performed by an apparatus for measuring the distribution of fluorescence in the cell or cells, and
25 thereby any change in the distribution of fluorescence in the cell or cells, which includes at a minimum the following component parts: (a) a light source, (b) a method for selecting the wavelength(s) of light from the source which will excite the fluorophore, (c) a method for directing the excitation light to the specimen, collecting the emitted fluorescence in a spatially resolved fashion, and forming an image from this fluorescence emission, (e) a bench or stand which holds the container of the cells being measured in a predetermined geometry with respect to the series of optical elements, and a detector for

record the spatially resolved fluorescence in the form of an image, (g) a computer or electronic system and associated software to acquire and store the recorded images, and to compute the degree of redistribution from the recorded images.

In a preferred embodiment of the invention the apparatus system is automated. In one embodiment the components in d and e mentioned above comprise a fluorescence microscope.
5 In one embodiment the component in f mentioned above is a CCD camera.

In one embodiment the image is formed and recorded by an optical scanning system.

In one embodiment a liquid addition system is used to add a known or unknown compound to any or all of the cells in the cell holder at a time determined in advance. Preferably, the
10 liquid addition system is under the control of the computer or electronic system. Such an automated system can be used for a screening program due to its ability to generate results from a larger number of test compounds than a human operator could generate using the apparatus in a manual fashion.

15 **Quantitation of the influence**

The recording of the variation or result with respect to light emitted from the luminophore is performed by recording the spatially distributed light as one or more digital images, and the processing of the recorded variation to reduce it to one or more numbers representative of the degree of redistribution comprises a digital image processing procedure or combination
20 of digital image processing procedures. The quantitative information which is indicative of the degree of the cellular response to the influence or the result of the influence on the intracellular pathway is extracted from the recording or recordings according to a predetermined calibration based on responses or results, recorded in the same manner, to known degrees of a relevant specific influence. This calibration procedure is developed according to principles
25 described below (Developing an Image-based Assay Technique). Specific descriptions of the procedures for particular assays are given in the examples.

While the stepwise procedure necessary to reduce the image or images to a number representative of the influence or the result of the influence on the intracellular pathway is described below, the individual steps are point operations such as addition, subtraction, ratioing, and thresholding, digital filtering methods such as smoothing, sharpening, and edge detection, spatial frequency methods such as Fourier filtering, image cross-correlation and image autocorrelation, object finding and object extraction, and various

and colour space manipulations for visualisation. In addition to the algorithmic procedures, heuristic methods such as neural networks may also be used.

Nucleic acid constructs

5 The nucleic acid constructs used in the present invention encode in their nucleic acid sequences fusion polypeptides comprising a biologically active polypeptide that is a component of an intracellular signalling pathway, or a part thereof, and a GFP, preferably an F64L mutant of GFP, N- or C-terminally fused, optionally via a peptide linker, to the biologically active polypeptide or part thereof.

10 In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a protein kinase or a phosphatase.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a transcription factor or a part thereof which changes cellular localisation upon activation.

15 In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a protein, or a part thereof, which is associated with the cytoskeletal network and which changes cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a protein kinase or a part thereof which changes cellular localisation upon activation.

20 In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a serine/threonine protein kinase or a part thereof capable of changing intracellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a tyrosine protein kinase or a part thereof capable of changing intracellular localisation upon activation.

25 In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a phospholipid-dependent serine/threonine protein kinase or a part thereof capable of changing intracellular localisation upon activation.

30 In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a cAMP-dependent protein kinase or a part thereof capable of changing cellular localisation upon activation. In a preferred embodiment the biologically active polypeptide encoded by the nucleic acid construct is a PKA α -F64L-S6BT-GFP fusion.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a cGMP-dependent protein kinase or a part thereof capable of changing cellular localisation upon activation.

5 In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a calmodulin-dependent serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a mitogen-activated serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation. In preferred embodiments the biologically active polypeptide encoded by the nucleic acid constructs are an ERK1-F64L-S65T-GFP fusion or an EGFP-ERK1 fusion.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a cyclin-dependent serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

15 In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a protein phosphatase or a part thereof capable of changing cellular localisation upon activation.

In one preferred embodiment of the invention the nucleic acid constructs may be DNA constructs.

20 In one embodiment the biologically active polypeptide encoded by the nucleic acid construct In one embodiment the gene encoding GFP in the nucleic acid construct is derived from *Aequorea victoria*. In a preferred embodiment the gene encoding GFP in the nucleic acid construct is EGFP or a GFP variant selected from F64L-GFP, F64L-Y66H-GFP and F64L-S65T-GFP.

25 In preferred embodiments of the invention the DNA constructs which can be identified by any of the DNA sequences shown in SEQ ID NO: 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398, 400, 402, 404, 406, 408, 410, 412, 414, 416, 418, 420, 422, 424, 426, 428, 430, 432, 434, 436, 438, 440, 442, 444, 446, 448, 450, 452, 454, 456, 458, 460, 462, 464, 466, 468, 470, 472, 474, 476, 478, 480, 482, 484, 486, 488, 490, 492, 494, 496, 498, 500, 502, 504, 506, 508, 510, 512, 514, 516, 518, 520, 522, 524, 526, 528, 530, 532, 534, 536, 538, 540, 542, 544, 546, 548, 550, 552, 554, 556, 558, 560, 562, 564, 566, 568, 570, 572, 574, 576, 578, 580, 582, 584, 586, 588, 590, 592, 594, 596, 598, 600, 602, 604, 606, 608, 610, 612, 614, 616, 618, 620, 622, 624, 626, 628, 630, 632, 634, 636, 638, 640, 642, 644, 646, 648, 650, 652, 654, 656, 658, 660, 662, 664, 666, 668, 670, 672, 674, 676, 678, 680, 682, 684, 686, 688, 690, 692, 694, 696, 698, 700, 702, 704, 706, 708, 710, 712, 714, 716, 718, 720, 722, 724, 726, 728, 730, 732, 734, 736, 738, 740, 742, 744, 746, 748, 750, 752, 754, 756, 758, 760, 762, 764, 766, 768, 770, 772, 774, 776, 778, 780, 782, 784, 786, 788, 790, 792, 794, 796, 798, 800, 802, 804, 806, 808, 810, 812, 814, 816, 818, 820, 822, 824, 826, 828, 830, 832, 834, 836, 838, 840, 842, 844, 846, 848, 850, 852, 854, 856, 858, 860, 862, 864, 866, 868, 870, 872, 874, 876, 878, 880, 882, 884, 886, 888, 890, 892, 894, 896, 898, 900, 902, 904, 906, 908, 910, 912, 914, 916, 918, 920, 922, 924, 926, 928, 930, 932, 934, 936, 938, 940, 942, 944, 946, 948, 950, 952, 954, 956, 958, 960, 962, 964, 966, 968, 970, 972, 974, 976, 978, 980, 982, 984, 986, 988, 990, 992, 994, 996, 998, 1000, 1002, 1004, 1006, 1008, 1010, 1012, 1014, 1016, 1018, 1020, 1022, 1024, 1026, 1028, 1030, 1032, 1034, 1036, 1038, 1040, 1042, 1044, 1046, 1048, 1050, 1052, 1054, 1056, 1058, 1060, 1062, 1064, 1066, 1068, 1070, 1072, 1074, 1076, 1078, 1080, 1082, 1084, 1086, 1088, 1090, 1092, 1094, 1096, 1098, 1100, 1102, 1104, 1106, 1108, 1110, 1112, 1114, 1116, 1118, 1120, 1122, 1124, 1126, 1128, 1130, 1132, 1134, 1136, 1138, 1140, 1142, 1144, 1146, 1148, 1150, 1152, 1154, 1156, 1158, 1160, 1162, 1164, 1166, 1168, 1170, 1172, 1174, 1176, 1178, 1180, 1182, 1184, 1186, 1188, 1190, 1192, 1194, 1196, 1198, 1200, 1202, 1204, 1206, 1208, 1210, 1212, 1214, 1216, 1218, 1220, 1222, 1224, 1226, 1228, 1230, 1232, 1234, 1236, 1238, 1240, 1242, 1244, 1246, 1248, 1250, 1252, 1254, 1256, 1258, 1260, 1262, 1264, 1266, 1268, 1270, 1272, 1274, 1276, 1278, 1280, 1282, 1284, 1286, 1288, 1290, 1292, 1294, 1296, 1298, 1300, 1302, 1304, 1306, 1308, 1310, 1312, 1314, 1316, 1318, 1320, 1322, 1324, 1326, 1328, 1330, 1332, 1334, 1336, 1338, 1340, 1342, 1344, 1346, 1348, 1350, 1352, 1354, 1356, 1358, 1360, 1362, 1364, 1366, 1368, 1370, 1372, 1374, 1376, 1378, 1380, 1382, 1384, 1386, 1388, 1390, 1392, 1394, 1396, 1398, 1400, 1402, 1404, 1406, 1408, 1410, 1412, 1414, 1416, 1418, 1420, 1422, 1424, 1426, 1428, 1430, 1432, 1434, 1436, 1438, 1440, 1442, 1444, 1446, 1448, 1450, 1452, 1454, 1456, 1458, 1460, 1462, 1464, 1466, 1468, 1470, 1472, 1474, 1476, 1478, 1480, 1482, 1484, 1486, 1488, 1490, 1492, 1494, 1496, 1498, 1500, 1502, 1504, 1506, 1508, 1510, 1512, 1514, 1516, 1518, 1520, 1522, 1524, 1526, 1528, 1530, 1532, 1534, 1536, 1538, 1540, 1542, 1544, 1546, 1548, 1550, 1552, 1554, 1556, 1558, 1560, 1562, 1564, 1566, 1568, 1570, 1572, 1574, 1576, 1578, 1580, 1582, 1584, 1586, 1588, 1590, 1592, 1594, 1596, 1598, 1600, 1602, 1604, 1606, 1608, 1610, 1612, 1614, 1616, 1618, 1620, 1622, 1624, 1626, 1628, 1630, 1632, 1634, 1636, 1638, 1640, 1642, 1644, 1646, 1648, 1650, 1652, 1654, 1656, 1658, 1660, 1662, 1664, 1666, 1668, 1670, 1672, 1674, 1676, 1678, 1680, 1682, 1684, 1686, 1688, 1690, 1692, 1694, 1696, 1698, 1700, 1702, 1704, 1706, 1708, 1710, 1712, 1714, 1716, 1718, 1720, 1722, 1724, 1726, 1728, 1730, 1732, 1734, 1736, 1738, 1740, 1742, 1744, 1746, 1748, 1750, 1752, 1754, 1756, 1758, 1760, 1762, 1764, 1766, 1768, 1770, 1772, 1774, 1776, 1778, 1780, 1782, 1784, 1786, 1788, 1790, 1792, 1794, 1796, 1798, 1800, 1802, 1804, 1806, 1808, 1810, 1812, 1814, 1816, 1818, 1820, 1822, 1824, 1826, 1828, 1830, 1832, 1834, 1836, 1838, 1840, 1842, 1844, 1846, 1848, 1850, 1852, 1854, 1856, 1858, 1860, 1862, 1864, 1866, 1868, 1870, 1872, 1874, 1876, 1878, 1880, 1882, 1884, 1886, 1888, 1890, 1892, 1894, 1896, 1898, 1900, 1902, 1904, 1906, 1908, 1910, 1912, 1914, 1916, 1918, 1920, 1922, 1924, 1926, 1928, 1930, 1932, 1934, 1936, 1938, 1940, 1942, 1944, 1946, 1948, 1950, 1952, 1954, 1956, 1958, 1960, 1962, 1964, 1966, 1968, 1970, 1972, 1974, 1976, 1978, 1980, 1982, 1984, 1986, 1988, 1990, 1992, 1994, 1996, 1998, 2000, 2002, 2004, 2006, 2008, 2010, 2012, 2014, 2016, 2018, 2020, 2022, 2024, 2026, 2028, 2030, 2032, 2034, 2036, 2038, 2040, 2042, 2044, 2046, 2048, 2050, 2052, 2054, 2056, 2058, 2060, 2062, 2064, 2066, 2068, 2070, 2072, 2074, 2076, 2078, 2080, 2082, 2084, 2086, 2088, 2090, 2092, 2094, 2096, 2098, 2100, 2102, 2104, 2106, 2108, 2110, 2112, 2114, 2116, 2118, 2120, 2122, 2124, 2126, 2128, 2130, 2132, 2134, 2136, 2138, 2140, 2142, 2144, 2146, 2148, 2150, 2152, 2154, 2156, 2158, 2160, 2162, 2164, 2166, 2168, 2170, 2172, 2174, 2176, 2178, 2180, 2182, 2184, 2186, 2188, 2190, 2192, 2194, 2196, 2198, 2200, 2202, 2204, 2206, 2208, 2210, 2212, 2214, 2216, 2218, 2220, 2222, 2224, 2226, 2228, 2230, 2232, 2234, 2236, 2238, 2240, 2242, 2244, 2246, 2248, 2250, 2252, 2254, 2256, 2258, 2260, 2262, 2264, 2266, 2268, 2270, 2272, 2274, 2276, 2278, 2280, 2282, 2284, 2286, 2288, 2290, 2292, 2294, 2296, 2298, 2300, 2302, 2304, 2306, 2308, 2310, 2312, 2314, 2316, 2318, 2320, 2322, 2324, 2326, 2328, 2330, 2332, 2334, 2336, 2338, 2340, 2342, 2344, 2346, 2348, 2350, 2352, 2354, 2356, 2358, 2360, 2362, 2364, 2366, 2368, 2370, 2372, 2374, 2376, 2378, 2380, 2382, 2384, 2386, 2388, 2390, 2392, 2394, 2396, 2398, 2400, 2402, 2404, 2406, 2408, 2410, 2412, 2414, 2416, 2418, 2420, 2422, 2424, 2426, 2428, 2430, 2432, 2434, 2436, 2438, 2440, 2442, 2444, 2446, 2448, 2450, 2452, 2454, 2456, 2458, 2460, 2462, 2464, 2466, 2468, 2470, 2472, 2474, 2476, 2478, 2480, 2482, 2484, 2486, 2488, 2490, 2492, 2494, 2496, 2498, 2500, 2502, 2504, 2506, 2508, 2510, 2512, 2514, 2516, 2518, 2520, 2522, 2524, 2526, 2528, 2530, 2532, 2534, 2536, 2538, 2540, 2542, 2544, 2546, 2548, 2550, 2552, 2554, 2556, 2558, 2560, 2562, 2564, 2566, 2568, 2570, 2572, 2574, 2576, 2578, 2580, 2582, 2584, 2586, 2588, 2590, 2592, 2594, 2596, 2598, 2600, 2602, 2604, 2606, 2608, 2610, 2612, 2614, 2616, 2618, 2620, 2622, 2624, 2626, 2628, 2630, 2632, 2634, 2636, 2638, 2640, 2642, 2644, 2646, 2648, 2650, 2652, 2654, 2656, 2658, 2660, 2662, 2664, 2666, 2668, 2670, 2672, 2674, 2676, 2678, 2680, 2682, 2684, 2686, 2688, 2690, 2692, 2694, 2696, 2698, 2700, 2702, 2704, 2706, 2708, 2710, 2712, 2714, 2716, 2718, 2720, 2722, 2724, 2726, 2728, 2730, 2732, 2734, 2736, 2738, 2740, 2742, 2744, 2746, 2748, 2750, 2752, 2754, 2756, 2758, 2760, 2762, 2764, 2766, 2768, 2770, 2772, 2774, 2776, 2778, 2780, 2782, 2784, 2786, 2788, 2790, 2792, 2794, 2796, 2798, 2800, 2802, 2804, 2806, 2808, 2810, 2812, 2814, 2816, 2818, 2820, 2822, 2824, 2826, 2828, 2830, 2832, 2834, 2836, 2838, 2840, 2842, 2844, 2846, 2848, 2850, 2852, 2854, 2856, 2858, 2860, 2862, 2864, 2866, 2868, 2870, 2872, 2874, 2876, 2878, 2880, 2882, 2884, 2886, 2888, 2890, 2892, 2894, 2896, 2898, 2900, 2902, 2904, 2906, 2908, 2910, 2912, 2914, 2916, 2918, 2920, 2922, 2924, 2926, 2928, 2930, 2932, 2934, 2936, 2938, 2940, 2942, 2944, 2946, 2948, 2950, 2952, 2954, 2956, 2958, 2960, 2962, 2964, 2966, 2968, 2970, 2972, 2974, 2976, 2978, 2980, 2982, 2984, 2986, 2988, 2990, 2992, 2994, 2996, 2998, 3000, 3002, 3004, 3006, 3008, 3010, 3012, 3014, 3016, 3018, 3020, 3022, 3024, 3026, 3028, 3030, 3032, 3034, 3036, 3038, 3040, 3042, 3044, 3046, 3048, 3050, 3052, 3054, 3056, 3058, 3060, 3062, 3064, 3066, 3068, 3070, 3072, 3074, 3076, 3078, 3080, 3082, 3084, 3086, 3088, 3090, 3092, 3094, 3096, 3098, 3100, 3102, 3104, 3106, 3108, 3110, 3112, 3114, 3116, 3118, 3120, 3122, 3124, 3126, 3128, 3130, 3132, 3134, 3136, 3138, 3140, 3142, 3144, 3146, 3148, 3150, 3152, 3154, 3156, 3158, 3160, 3162, 3164, 3166, 3168, 3170, 3172, 3174, 3176, 3178, 3180, 3182, 3184, 3186, 3188, 3190, 3192, 3194, 3196, 3198, 3200, 3202, 3204, 3206, 3208, 3210, 3212, 3214, 3216, 3218, 3220, 3222, 3224, 3226, 3228, 3230, 3232, 3234, 3236, 3238, 3240, 3242, 3244, 3246, 3248, 3250, 3252, 3254, 3256, 3258, 3260, 3262, 3264, 3266, 3268, 3270, 3272, 3274, 3276, 3278, 3280, 3282, 3284, 3286, 3288, 3290, 3292, 3294, 3296, 3298, 3300, 3302, 3304, 3306, 3308, 3310, 3312, 3314, 3316, 3318, 3320, 3322, 3324, 3326, 3328, 3330, 3332, 3334, 3336, 3338, 3340, 3342, 3344, 3346, 3348, 3350, 3352, 3354, 3356, 3358, 3360, 3362, 3364, 3366, 3368, 3370, 3372, 3374, 3376, 3378, 3380, 3382, 3384, 3386, 3388, 3390, 3392, 3394, 3396, 3398, 3400, 3402, 3404, 3406, 3408, 3410, 3412, 3414, 3416, 3418, 3420, 3422, 3424, 3426, 3428, 3430, 3432, 3434, 3436, 3438, 3440, 3442, 3444, 3446, 3448, 3450, 3452, 3454, 3456, 3458, 3460, 3462, 3464, 3466, 3468, 3470, 3472, 3474, 3476, 3478, 3480, 3482, 3484, 3486, 3488, 3490, 3492, 3494, 3496, 3498, 3500, 3502, 3504, 3506, 3508, 3510, 3512, 3514, 3516, 3518, 3520, 3522, 3524, 3526, 3528, 3530, 3532, 3534, 3536, 3538, 3540, 3542, 3544, 3546, 3548, 3550, 3552, 3554, 3556, 3558, 3560, 3562, 3564, 3566, 3568, 3570, 3572, 3574, 3576, 3578, 3580, 3582, 3584, 3586, 3588, 3590, 3592, 3594, 3596, 3598, 3600, 3602, 3604, 3606, 3608, 3610, 3612, 3614, 3616, 3618, 3620, 3622, 3624, 3626, 3628, 3630, 3632, 3634, 3636, 3638, 3640, 3642, 3644, 3646, 3648, 3650, 3652, 3654, 3656, 3658, 3660, 3662, 3664, 3666, 3668, 3670, 3672, 3674, 3676, 3678, 3680, 3682, 3684, 3686, 3688, 3690, 3692, 3694, 3696, 3698, 3700, 3702, 3704, 3706, 3708, 3710, 3712, 3714, 3716, 3718, 3720, 3722, 3724, 3726, 3728, 3730, 3732, 3734, 3736, 3738, 3740, 3742, 3744, 3746, 3748, 3750, 3752, 3754, 3756, 3758, 3760, 3762, 3764, 3766, 3768, 3770, 3772, 3774, 3776, 3778, 3780, 3782, 3784, 3786, 3788, 3790, 3792, 3794, 3796, 3798, 3800, 3802, 3804, 3806, 3808, 3810, 3812, 3814, 3816, 3818, 3820, 3822, 3824, 3826, 3828, 3830, 3832, 3834, 3836, 3838, 3840, 3842, 3844, 3846, 3848, 3850, 3852, 3854, 3856, 3858, 3860, 3862, 3864, 3866, 3868, 3870, 3872, 3874, 3876, 3878, 3880, 3882, 3884, 3886, 3888, 3890, 3892, 3894, 3896, 3898, 3900, 3902, 3904, 3906, 3908, 3910, 3912, 3914, 3916, 3918, 3920, 3922, 3924, 3926, 3928, 3930, 3932, 3934, 3936, 3938, 3940, 3942, 3944, 3946, 3948, 3950, 3952, 3954, 3956, 3958, 3960, 3962, 3964, 3966, 3968, 3970, 3972, 3974, 3976, 3978, 3980, 3982, 3984, 3986, 3988, 3990, 3992, 3994, 3996, 3998, 4000, 4002, 4004, 4006, 4008, 4010, 4012, 4014, 4016, 4018, 4020, 4022, 4024, 4026, 4028, 4030, 4032, 4034, 4036, 4038, 4040, 4042, 4044, 4046, 4048, 4050, 4052, 4054, 4056, 4058, 4060, 4062, 4064, 4066, 4068, 4070, 4072, 4074, 4076, 4078, 4080, 4082, 4084, 4086, 4088, 4090, 4092, 4094,

Screening program

The present invention describes a method that may be used to establish a screening program for the identification of biologically active substances that directly or indirectly affects intracellular signalling pathways and because of this property are potentially useful as medicaments. Based on measurements in living cells of the redistribution of spatially resolved luminescence from luminophores which undergo a change in distribution upon activation or deactivation of an intracellular signalling pathway the result of the individual measurement of each substance being screened indicates its potential biological activity.

In one embodiment of the invention the screening program is used for the identification of a biologically toxic substance as defined herein that exerts its toxic effect by interfering with an intracellular signalling pathway. Based on measurements in living cells of the redistribution of spatially resolved luminescence from luminophores which undergo a change in distribution upon activation or deactivation of an intracellular signalling pathway the result of the individual measurement of each substance being screened indicates its potential biologically toxic activity. In one embodiment of a screening program a compound that modulates a component of an intracellular pathway as defined herein, can be found and the therapeutic amount of the compound estimated by a method according to the method of the invention. In a preferred embodiment the present invention leads to the discovery of a new way of treating a condition or disease related to the intracellular function of a biologically active polypeptide comprising administration to a patient suffering from said condition or disease of an effective amount of a compound which has been discovered by any method according to the invention. In another preferred embodiment of the invention a method is established for identification of a new drug target or several new drug targets among the group of biologically active polypeptides which are components of intracellular signalling pathways.

In another embodiment of the invention an individual treatment regimen is established for the selective treatment of a selected patient suffering from an ailment where the available medicaments used for treatment of the ailment are tested on a relevant primary cell or cells obtained from said patient from one or several tissues, using a method comprising transfecting the cell or cells with at least one fluorescent probe, exposing the cell or cells to said medicaments, and measuring the fluorescence of the cell or cells.

In another embodiment of the invention a method is established for the selective treatment of a selected patient, or for the identification of a new drug target or several new drug targets among the group of biologically active polypeptides which are components of intracellular signalling pathways, comprising: obtaining cells from said patient, or from a relevant tissue, or from a relevant cell line, transfecting the cells with at least one fluorescent probe, exposing the cells under conditions permitting the expression of said probes and exposing it to an array of the available medicaments, then comparing changes in fluorescence patterns or redistribution patterns of the fluorescent probes in the intact living cells or cells

detect the cellular response to the specific medicaments (obtaining a cellular action profile), then selecting one or more medicament or medicaments based on the desired activity and acceptable level of side effects and administering an effective amount of these medicaments to the selected patient.

5

Back-tracking of a signal transduction pathway

The present invention describes a method that may be used to establish a screening program for back-tracking signal transduction pathways as defined herein. In one embodiment the screening program is used to establish more precisely at which level one or several
10 compounds affect a specific signal transduction pathway by successively or in parallel testing the influence of the compound or compounds on the redistribution of spatially resolved luminescence from several of the luminophores which undergo a change in distribution upon activation or deactivation of the intracellular signalling pathway under study.

15 Construction and testing of probes

In general, a probe, i.e. a "GeneX"-GFP fusion or a GFP-"GeneX" fusion, is constructed using PCR with "GeneX"-specific primers followed by a cloning step to fuse "GeneX" in frame with GFP. The fusion may contain a short vector derived sequence between "GeneX" and GFP (e.g. part of a multiple cloning site region in the plasmid) resulting in a peptide linker between "GeneX" and GFP in the resulting fusion protein.
20

Detailed stepwise procedure:

- Identifying the sequence of the gene. This is most readily done by searching a depository of genetic information, e.g. the GenBank Sequence Database, which is widely available and
25 routinely used by molecular biologists. In the specific examples below the GenBank Accession number of the gene in question is provided.

After the sequence of the gene has been determined, inspection of the sequence of the gene allows design of gene-specific primers to be used in a PCR reaction. Typically, the top-strand primer encompasses the ATG start codon of the gene and the following ca. 20 nucleotides, while the
30 bottom-strand primer encompasses the stop codon and the ca. 20 preceding nucleotides.

the gene is to be fused behind GFP, i.e. a GFP-"GeneX" fusion. If the gene is to be fused in front of GFP, i.e. a "GeneX"-GFP fusion, a stop codon must be avoided. Optionally, the full length sequence of GeneX may not be used in the fusion, but merely the part which localizes and redistributes like GeneX in response to a signal.

5

In addition to gene-specific sequences, the primers contain at least one recognition sequence for a restriction enzyme, to allow subsequent cloning of the PCR product. The sites are chosen so that they are unique in the PCR product and compatible with sites in the cloning vector. Furthermore, it may be necessary to include an exact number of nucleotides between
10 the restriction enzyme site and the gene-specific sequence in order to establish the correct reading frame of the fusion gene and/or a translation initiation consensus sequence. Lastly, the primers always contain a few nucleotides in front of the restriction enzyme site to allow efficient digestion with the enzyme.

15 -Identifying a source of the gene to be amplified. In order for a PCR reaction to produce a product with gene-specific primers, the gene-sequence must initially be present in the reaction, e.g. in the form of cDNA. Information in GenBank or the scientific literature will usually indicate in which tissue(s) the gene is expressed, and cDNA libraries from a great variety of tissues or cell types from various species are commercially available, e.g. from Clontech
20 (Palo Alto), Stratagene (La Jolla) and Invitrogen (San Diego). Many genes are also available in cloned form from The American Type Tissue Collection (Virginia).

- Optimizing the PCR reaction. Several factors are known to influence the efficiency and specificity of a PCR reaction, including the annealing temperature of the primers, the concentration of ions, notably Mg^{2+} and K^{+} , present in the reaction, as well as pH of the reaction.
25 If the result of a PCR reaction is deemed unsatisfactory, it might be because the parameters mentioned above are not optimal. Various annealing temperatures should be tested, e.g. on a PCR machine with a 10°C

gradient system from

Applied Biosystems

- Cloning the PCR product. The vector into which the amplified gene product will be cloned and fused with GFP will already have been taken into consideration when the primers were designed. When choosing a vector, one should at least consider in which cell types the probe subsequently will be expressed, so that the promoter controlling expression of the probe is compatible with the cells. Most expression vectors also contain one or more selective markers, e.g. conferring resistance to a drug, which is a useful feature when one wants to make stable transfectants. The selective marker should also be compatible with the cells to be used.
- 10 The actual cloning of the PCR product should present no difficulty as it typically will be a one-step cloning of a fragment digested with two different restriction enzymes into a vector digested with the same two enzymes. If the cloning proves to be problematic, it may be because the restriction enzymes did not work well with the PCR fragment. In this case one could add longer extensions to the end of the primers to overcome a possible difficulty of digestion close to a fragment end, or one could introduce an intermediate cloning step not based on restriction enzyme digestion. Several companies offer systems for this approach, e.g. Invitrogen (San Diego) and Clontech (Palo Alto).

- Once the gene has been cloned and, in the process, fused with the GFP gene, the resulting product, usually a plasmid, should be carefully checked to make sure it is as expected. The most exact test would be to obtain the nucleotide sequence of the fusion-gene.

Testing the probe

- Once a DNA construct for a probe has been generated, its functionality and usefulness may be tested by subjecting it to the following tests:

- Transfecting it into cells capable of

expressing GFP and measuring the resulting fluorescence intensity and the sub-cellular localization.

The intensity should usually be at least as strong as that of unfused GFP in the cells. If it is not, the sequence or quality of the probe-DNA might be faulty, and should be carefully checked.

- 5 The sub-cellular localization is an indication of whether the probe is likely to perform well. If it localizes as expected for the gene in question, e.g. is excluded from the nucleus, it can immediately go on to a functional test. If the probe is not localized soon after the transfection procedure, it may be because of overexpression at this point in time, as the cell typically will have taken of very many copies of the plasmid, and localization will occur in time, e.g. within
- 10 a few weeks, as plasmid copy number and expression level decreases. If localization does not occur after prolonged time, it may be because the fusion to GFP has destroyed a localization function, e.g. masked a protein sequence essential for interaction with its normal cellular anchor-protein. In this case the opposite fusion might work, e.g. if GeneX-GFP does not
- 15 GFP. If this does not work, the proximity of GFP at either end might be a problem, and it could be attempted to increase the distance by incorporating a longer linker between GeneX and GFP in the DNA construct.

If there is no prior knowledge of localization, and no localization is observed, it may be because the probe should not be localized at this point, because such is the nature of the protein fused to GFP. It should then be subjected to a functional test.

In a functional test, the cells expressing the probe are treated with at least one compound known to perturb, usually by activating, the signalling pathway on which the probe is expected to report by redistributing itself within the cell. If the redistribution is as expected, e.g. if prior knowledge tell that it should translocate from location X to location Y, it has passed the

25 first critical test. In this case it can go on to further characterization and quantification of the response.

If it does not perform as expected, it may be because the cell lacks at least one component of the signalling pathway, e.g. a cell surface receptor.

In such cases, for instance, one should identify other cell types for the testing process where these potential problems would not apply.

If there is no prior knowledge about the pattern of redistribution, the analysis of the redistribution will have to be done in greater depth to identify what the essential and indicative features are, and when this is clear, it can go on to further characterization and quantification of the response. If no feature of redistribution can be identified, the problem might be as mentioned above, and the probe should be retested under more optimal cellular conditions.

If the probe does not perform under optimal cellular conditions it's back to the drawing board.

Developing an image-based assay technique

The process of developing an image-based redistribution assay begins with either the unplanned experimental observation that a redistribution phenomenon can be visualised, or the design of a probe specifically to follow a redistribution phenomenon already known to occur. In either event, the first and best exploratory technique is for a trained scientist or technician to observe the phenomenon. Even with the rapid advances in computing technology, the human eye-brain combination is still the most powerful pattern recognition system known, and requires no advance knowledge of the system in order to detect potentially interesting and useful patterns in raw data. This is especially if those data are presented in the form of images, which are the natural "data type" for human visual processing. Because human visual processing operates most effectively in a relatively narrow frequency range, i.e., we cannot see either very fast or very slow changes in our visual field, it may be necessary to record the data and play it back with either time dilation or time compression.

Some luminescence phenomena cannot be seen directly by the human eye. Examples include polarization and fluorescence lifetime. However, with suitable filters or detectors, these signals can be recorded as images or sequences of images and displayed to the human in the fashion just described. In this way, patterns can be detected and the same methods can be applied.

Once the redistribution has been determined to be a reproducible phenomenon, one or more data sets are generated for the purpose of developing a procedure for extracting qualitative information.

As the assay is refined, it may become an iterative process. If it may be necessary to develop a quantitative procedure in order to assess the effect on the assay of manipulating the assay conditions.

The data sets are examined by a person or persons with knowledge of the biological phenomenon and skill in the application of image processing techniques. The goal of this exercise is to determine or at least propose a method which will reduce the image or sequence of images constituting the record of a "response" to a value corresponding to the degree of the response. Using either interactive image processing software or an image processing toolbox and a programming language, the method is encoded as a procedure or algorithm which takes the image or images as input and generates the degree of response (in any units) as its output. Some of the criteria for evaluating the validity of a particular procedure are:

- Does the degree of the response vary in a biologically significant fashion, i.e., does it show the known or putative dependence on the concentration of the stimulating agent or condition?
- Is the degree of response reproducible, i.e., does the same concentration or level of stimulating agent or condition give the same response with an acceptable variance?
- Is the dynamic range of the response sufficient for the purpose of the assay? If not, can a change in the procedure or one of its parameters improve the dynamic range?
- Does the procedure exhibit any clear "pathologies", i.e., does it give ridiculous values for the response if there are commonly occurring imperfections in the imaging process? Can these pathologies be eliminated, controlled, or accounted for?
- Can the procedure deal with the normal variation in the number and/or size of cells in an image?

In some cases the method may be obvious; in others, a number of possible procedures may suggest themselves. Even if one method appears clearly superior to others, optimisation of parameters may be required. The various procedures are applied to the data set and the criteria suggested above are determined, or the single procedure is applied repeatedly with adjustment of the parameter or parameters until the most satisfactory combination of signal, noise, range, etc. are arrived at. This is equivalent to the calibration of a measurement channel.

When the number of possible procedures and the value from an image are extremely large, and thus an intelligent approach must be taken to the initial step of reducing this number to a small, finite number of possible procedures. This is not to say that the procedure arrived at

necessarily the best procedure - but a global search for the best procedure is simply out of the question due to the sheer number of possibilities involved.

Image-based assays are no different than other assay techniques in that their usefulness is characterised by parameters such as the specificity for the desired component of the sample, the dynamic range, the variance, the sensitivity, the concentration range over which the assay will work, and other such parameters. While it is not necessary to characterise each and every one of these before using the assay, they represent the only way to compare one assay with another.

10 Example: Developing a Quantitative assay for GLUT4 Translocation

GLUT4 is a member of the class of glucose transporter molecules which are important in cellular glucose uptake. It is known to translocate to the plasma membrane under some conditions of stimulation of glucose uptake. The ability to visualize the glucose uptake response noninvasively, without actually measuring glucose uptake, would be a very useful assay for anyone looking for, for example, treatments for type II diabetes.

A CHO cell line which stably expressed the human insulin receptor was used as the basis for a new cell line which stably expressed a fusion between GLUT4 and GFP. This cell line was expected to show translocation of GLUT4 to the plasma membrane as visualized by the movement of the GFP. The translocation could definitely be seen in the form of the appearance of local increases in the fluorescence in regions of the plasma membrane which had a characteristic shape or pattern. This is shown in Figure 12.

These objects became known as "snirclles", and the phenomenon of their appearance as "snircling". In order to quantitate their appearance, a method had to be found to isolate them as objects in the image field, and then enumerate them, measure their area, or determine some parameter about them which correlated in a dose-dependent fashion with the concentration of insulin to which the cells had been exposed. In order to separate the snirclles, a binarization procedure was applied in which one copy of the image smoothed with a relatively severe gaussian kernel

was subtracted from the original image. The resultant image was then normalized to its min-max range, and an automatic threshold was applied to divide the image into two levels. The thresholded image contains a background of one value all found object with another value. The found objects were first filtered through a filter to remove objects that

large and far too small to be snirclcs. The remaining objects, which represent snirclcs and other artifacts from the image with approximately the same size and intensity characteristics as snirclcs, are passed into a classification procedure which has been previously trained with many images of snirclcs to recognize snirclcs and exclude the other artifacts. The result of this procedure is a binary image which shows only the found snirclcs to the degree to which the classification procedure can accurately identify them. The total area of the snirclcs is then summed and this value is the quantitative measure of the degree of snircling for that image.

10 **Definitions:**

In the present specification and claims, the term "an influence" covers any influence to which the cellular response comprises a redistribution. Thus, e.g., heating, cooling, high pressure, low pressure, humidifying, or drying are influences on the cellular response on which the resulting redistribution can be quantified, but as mentioned above, perhaps the most important influences are the influences of contacting or incubating the cell or cells with substances which are known or suspected to exert an influence on the cellular response involving a redistribution contribution. In another embodiment of the invention the influence could be substances from a compound drug library.

20 In the present context, the term "green fluorescent protein" is intended to indicate a protein which, when expressed by a cell, emits fluorescence upon exposure to light of the correct excitation wavelength (cf. [(Chalfie *et al.* 1994)]). In the following, GFP in which one or more amino acids have been substituted, inserted or deleted is most often termed "modified GFP". "GFP" as used herein includes wild-type GFP derived from the jelly fish *Aequorea victoria* and modifications of GFP, such as the blue fluorescent variant of GFP disclosed by Heim et al. (1994). Proc.Natl.Acad.Sci. 91:12501, and other modifications that change the spectral properties of the GFP fluorescence, or modifications that exhibit increased fluorescence when expressed in cells at a temperature of 37°C.

DEFINITIONS

1. A green fluorescent protein derived from *Aequorea* Green Fluorescent Protein (GFP) or any functional analogue thereof, wherein the amino acid in position 1 upstream from the chromophore has been mutated to provide an increase of fluorescence intensity when the

fluorescent protein of the invention is expressed in cells. Preferred GFP variants are F64L-GFP, F64L-Y66H-GFP and F64L-S65T-GFP. An especially preferred variant of GFP for use in all the aspects of this invention is EGFP (DNA encoding EGFP which is a F64L-S65T variant with codons optimized for expression in mammalian cells is available from Clontech, Palo Alto, plasmids containing the EGFP DNA sequence, cf. GenBank Acc. Nos. U55762, U55763).

The term "intracellular signalling pathway" and "signal transduction pathway" are intended to indicate the coordinated intracellular processes whereby a living cell transduce an external or internal signal into cellular responses. Said signal transduction will involve an enzymatic reaction said enzymes include but are not limited to protein kinases, GTPases, ATPases, protein phosphatases, phospholipases. The cellular responses include but are not limited to gene transcription, secretion, proliferation, mechanical activity, metabolic activity, cell death.

The term "second messenger" is used to indicate a low molecular weight component involved in the early events of intracellular signal transduction pathways.

The term "luminophore" is used to indicate a chemical substance which has the property of emitting light either inherently or upon stimulation with chemical or physical means. This includes but is not limited to fluorescence, bioluminescence, phosphorescence, chemiluminescence.

The term "mechanically intact living cell" is used to indicate a cell which is considered living according to standard criteria for that particular type of cell such as maintenance of normal membrane potential, energy metabolism, proliferative capability, and has not experienced any physically invasive treatment designed to introduce external substances into the cell such as microinjection.

The term "intracellular component" as measured by a change in the luminescence properties or distribution, is used to indicate that said redistribution can be explained in terms of the underlying biological phenomenon which gives rise to the redistribution.

Th terms "image processing" and "image analysis" are used to describe a large family of digital data analysis techniques or combination of such techniques which reduce ordered arrays of numbers (images) to quantitative information describing those ordered arrays of numbers. When said ordered arrays of numbers represent measured values from a physical process, the quantitative information derived is therefore a measure of the physical process.

The term "fluorescent probe" is used to indicate a fluorescent fusion polypeptide comprising a GFP or any functional part thereof which is N- or C-terminally fused to a biologically active polypeptide as defined herein, optionally via a peptide linker consisting of one or more amino acid residues, where the size of the linker peptide in itself is not critical as long as the desired functionality of the fluorescent probe is maintained. A fluorescent probe according to the invention is expressed in a cell and basically mimics the physiological behaviour of the biologically active polypeptide moiety of the fusion polypeptide.

The term "mammalian cell" is intended to indicate any living cell of mammalian origin. The cell may be an established cell line, many of which are available from The American Type Culture Collection (ATCC, Virginia, USA) or a primary cell with a limited life span derived from a mammalian tissue, including tissues derived from a transgenic animal, or a newly established immortal cell line derived from a mammalian tissue including transgenic tissues, or a hybrid cell or cell line derived by fusing different celltypes of mammalian origin e.g. hybridoma cell lines. The cells may optionally express one or more non-native gene products, e.g. receptors, enzymes, enzyme substrates, prior to or in addition to the fluorescent probe. Preferred cell lines include but are not limited to those of fibroblast origin, e.g. BHK, CHO, BALB, or of endothelial origin, e.g. HUVEC, BAE (bovine artery endothelial), CPAE (cow pulmonary artery endothelial) or of pancreatic origin, e.g. RIN, INS-1, MIN6, bTC3, aTC6, bTC6, HIT, or of hematopoietic origin, e.g. adipocyte origin, e.g. 3T3-L1, neuronal/neuroendocrine origin, e.g. AtT20, PC12, GH3, muscle origin, e.g. SKMC, A10, C2C12, renal origin, e.g. HEK 293, LLC-PK1.

As indicated above, the term "hybrid protein" in this case at least a portion of the green fluorescent protein, and at least a portion of a catalytic and/or regulatory domain of a protein kinase. Furthermore a hybrid polypeptide is intended to indicate a fusion polypeptide comprising a

GFP or at least a portion of the green fluorescent protein that contains a functional fluorophore, and at least a portion of a biologically active polypeptide as defined herein provided that said fusion is not the PKC α -GFP, PKC γ -GFP, and PKC ϵ -GFP disclosed by Schmidt et al. and Sakai et al., respectively. Thus, GFP may be N- or C-terminally tagged to a biologically active polypeptide, optionally via a linker portion or linker peptide consisting of a sequence of one or more amino acids. The hybrid polypeptide or fusion polypeptide may act as a fluorescent probe in intact living cells carrying a DNA sequence encoding the hybrid polypeptide under conditions permitting expression of said hybrid polypeptide.

- 10 The term "kinase" is intended to indicate an enzyme that is capable of phosphorylating a cellular component.

The term "protein kinase" is intended to indicate an enzyme that is capable of phosphorylating serine and/or threonine and/or tyrosine in peptides and/or proteins.

- 15 The term "phosphatase" is intended to indicate an enzyme that is capable of dephosphorylating phosphoserine and/or phosphothreonine and/or phosphotyrosine in peptides and/or proteins.

- In the present context, the term "biologically active polypeptide" is intended to indicate a polypeptide affecting intracellular processes upon activation, such as an enzyme which is active in intracellular processes or a portion thereof comprising a desired amino acid sequence which has a biological function or exerts a biological effect in a cellular system. In the polypeptide one or several amino acids may have been deleted, inserted or replaced to alter its biological function, e.g. by rendering a catalytic site inactive. Preferably, the biologically active polypeptide is selected from the group consisting of proteins taking part in an intracellular signalling pathway, such as enzymes involved in the intracellular phosphorylation and dephosphorylation processes including kinases, protein kinases and phosphatases.

herein, but not limited to, the term "biologically active polypeptide" is intended to indicate a polypeptide affecting intracellular processes upon activation, such as an enzyme which is active in intracellular processes or a portion thereof comprising a desired amino acid sequence which has a biological function or exerts a biological effect in a cellular system. In the polypeptide one or several amino acids may have been deleted, inserted or replaced to alter its biological function, e.g. by rendering a catalytic site inactive. Preferably, the biologically active polypeptide is selected from the group consisting of proteins taking part in an intracellular signalling pathway, such as enzymes involved in the intracellular phosphorylation and dephosphorylation processes including kinases, protein kinases and phosphatases.

termediary component in a signal transduction pathway. Included in this preferred group of biologically active polypeptides are cAMP dependent protein kinase A.

5 The term "a substance having biological activity" is intended to indicate any sample which has a biological function or exerts a biological effect in a cellular system. The sample may be a sample of a biological material such as a sample of a body fluid including blood, plasma, saliva, milk, urine, or a microbial or plant extract, an environmental sample containing pollutants including heavy metals or toxins, or it may be a sample containing a compound or mixture of compounds prepared by organic synthesis or genetic techniques.

10

The phrase "any change in fluorescence" means any change in absorption properties, such as wavelength and intensity, or any change in spectral properties of the emitted light, such as a change of wavelength, fluorescence lifetime, intensity or polarisation, or any change in the intracellular localisation of the fluorophore. It may thus be localised to a specific cellular component (e.g. organelle, membrane, cytoskeleton, molecular structure) or it may be evenly distributed throughout the cell or parts of the cell.

15

The phrase "back-tracking of a signal transduction pathway" is intended to indicate.

The term "organism" as used herein indicates any unicellular or multicellular organism preferably originating from the animal kingdom including protozoans, but also organisms that are members of the plant kingdoms, such as algae, fungi, bryophytes, and vascular plants are included in this definition.

20

The term "nucleic acid" is intended to indicate any type of poly- or oligonucleic acid sequence, such as a DNA sequence, a cDNA sequence, or an RNA sequence.

25

The term "biologically equivalent" as it relates to proteins is intended to mean that two proteins are functionally equivalent if they perform identical cellular functions in different cell types, or in different species. The term "biologically equivalent" as it relates to DNA is intended to mean that a test DNA sequence is functionally equivalent to a reference DNA sequence if they encode polypeptides that perform identical cellular functions in different cell types, or in different species. The term "biologically equivalent" as it relates to proteins is intended to mean that two proteins are functionally equivalent if they perform identical cellular functions in different cell types, or in different species. The term "biologically equivalent" as it relates to DNA is intended to mean that a test DNA sequence is functionally equivalent to a reference DNA sequence if they encode polypeptides that perform identical cellular functions in different cell types, or in different species. The term "biologically equivalent" as it relates to proteins is intended to mean that two proteins are functionally equivalent if they perform identical cellular functions in different cell types, or in different species. The term "biologically equivalent" as it relates to DNA is intended to mean that a test DNA sequence is functionally equivalent to a reference DNA sequence if they encode polypeptides that perform identical cellular functions in different cell types, or in different species.

30

ence encoding a polypeptide is equivalent to a second DNA sequence encoding a polypeptide if the functional proteins encoded by the two genes are biologically equivalent.

5 The phrase "back-tracking of a signal transduction pathway" is intended to indicate a process for defining more precisely at what level a signal transduction pathway is affected, either by the influence of chemical compounds or a disease state in an organism. Consider a specific signal transduction pathway represented by the bioactive polypeptides A - B - C - D, with signal transduction from A towards D. When investigating all components of this signal transduction pathway compounds or disease states that influence the activity or redistribution of only D can be considered to act on C or downstream of C whereas compounds or
10 disease states that influence the activity or redistribution of C and D, but not of A and B can be considered to act downstream of B.

The term "fixed cells" is used to mean cells treated with a cytological fixative such as glutaraldehyde or formaldehyde, treatments which serve to chemically cross-link and stabilize
15 soluble and insoluble proteins within the structure of the cell. Once in this state, such proteins cannot be lost from the structure of the now-dead cell.

20

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1. CHO cells expressing the PKAc-F64L-S65T-GFP hybrid protein have been treated in HAM's F12 medium with 50 mM forskolin at 37°C. The images of the GFP fluorescence in
25 these cells have been taken at different time intervals after treatment, which were: a) 40 seconds b) 60 seconds c) 70 seconds d) 80 seconds. The fluorescence changes from punctate to a more diffuse pattern.

Figure 2. Time-lapse analysis of forskolin induced PKAc-F64L-S65T-GFP redistribution. CHO cells, expressing the PKAc-F64L-S65T-GFP fusion protein were analysed by time-lapse fluorescence microscopy. Fluorescence micrographs were acquired at regular intervals from 2 min before to 8 min after the addition of agonist. The cells were challenged with 1 mM forskolin immediately after the upper left image was acquired (t=0). Frames were collected at the following times: i) 0, ii) 1, iii) 2, iv) 3, v) 4 and vi) 5 minutes. Scale bar 10 μ m.

Figure 3. Time-lapse analyses of PKAc-F64L-S65T-GFP redistribution in response to various agonists. The effects of 1 mM forskolin (A), 50 mM forskolin (B), 1mM dbcAMP (C) and 100 mM IBMX (D) (additions indicated by open arrows) on the localisation of the PKAc-F64L-S65T-GFP fusion protein were analysed by time-lapse fluorescence microscopy of CHO/PKAc-F64L-S65T-GFP cells. The effect of addition of 10 mM forskolin (open arrow), followed shortly by repeated washing with buffer (solid arrow), on the localisation of the PKAc-F64L-S65T-GFP fusion protein was analysed in the same cells (E). In a parallel experiment, the effect of adding 10 mM forskolin and 100 mM IBMX (open arrow) followed by repeated washing with buffer containing 100 mM IBMX (solid arrow) was analysed (F). Removing forskolin caused PKAc-F64L-S65T-GFP fusion protein to return to the cytoplasmic aggregates while this is prevented by the continued presence of IBMX (F). The effect of 100 nM glucagon (Fig 3G, open arrow) on the localisation of the PKAc-F64L-S65T-GFP fusion protein is also shown for BHK/GR, PKAc-F64L-S65T-GFP cells. The effect of 10 mM norepinephrine (H), solid arrow, on the localisation of the PKAc-F64L-S65T-GFP fusion protein was analysed similarly, in transiently transfected CHO, PKAc-F64L-S65T-GFP cells, pretreated with 10 mM forskolin, open arrow, to increase [cAMP]. N.B. in Fig 3H the x-axis counts the image numbers, with 12 seconds between images. The raw data of each experiment consisted of 60 fluorescence micrographs acquired at regular intervals including several images acquired before the addition of buffer or agonist. The charts (A-G) each show a quantification of the response seen through all the 60 images performed as described in analysis method 2. The x-axis represents the image number and the y-axis represents the percentage of cells with aggregates. The scale bar in the micrographs is 10 μ m. The charts are representative of three independent experiments. Scale bar 10 μ m.

Figure 4. Dose response curve (two experiments) for forskolin-induced redistribution of the PKAc-F64L-S65T-GFP fusion.

5

Figure 5. Time from initiation of a response to half maximal ($t_{1/2max}$) and maximal (t_{max}) PKAc-F64L-S65T-GFP redistribution. The data was extracted from curves such as that shown in "Figure 2." All $t_{1/2max}$ and t_{max} values are given as mean \pm SD and are based on a total of 26-30 cells from 2-3 independent experiments for each forskolin concentration. Since the observed
10 redistribution is sustained over time, the t_{max} values were taken as the earliest time point at which complete redistribution is reached. Note that the values do not relate to the degree of redistribution.

15 Figure 6. Parallel dose response analyses of forskolin induced cAMP elevation and PKAc-F64L-S65T-GFP redistribution. The effects of buffer or 5 increasing concentrations of forskolin on the localisation of the PKAc-F64L-S65T-GFP fusion protein in CHO/PKAc-F64L-S65T-GFP cells, grown in a 96 well plate, were analysed as described above. Computing the ratio of the SD's of fluorescence micrographs taken of the same field of cells, prior to and 30 min
20 after the addition of forskolin, gave a reproducible measure of PKAc-F64L-S65T-GFP redistribution. The graph shows the individual 48 measurements and a trace of their mean \pm s.e.m at each forskolin concentration. For comparison, the effects of buffer or 8 increasing concentrations of forskolin on [cAMP]_i was analysed by a scintillation proximity assay of cells grown under the same conditions. The graph shows a trace of the mean \pm s.e.m of 4
25 experiments expressed in arbitrary units.

Figure 7. BHK cells stably transfected with a cDNA encoding a GFP fused to a transiently expressed protein, PKAc-F64L-S65T-GFP, were treated with carbachol to induce a transient translocation of PKAc-F64L-S65T-GFP from the cytoplasm to the plasma membrane. Images were taken at the following times: a) 1 second before carbachol addition, b) 8.8 seconds after addition and c) 52.8 seconds after addition.

Figure 8. BHK cells stably transfected with the hM1 receptor and PKCa-F64L-S65T-GFP fusion were treated with carbachol (1 mM, 10 mM, 100 mM). In single cells intracellular $[Ca^{2+}]$ was monitored simultaneously with the redistribution of PKCa-F64L-S65T-GFP. Dashed line indicates the addition times of carbachol. The top panel shows changes in the intracellular Ca^{2+} concentration of individual cells with time for each treatment. The middle panel shows changes in the average cytoplasmic GFP fluorescence for individual cells against time for each treatment. The bottom panel shows changes in the fluorescence of the periphery of single cells, within regions that specifically include the circumferential edge of a cell as seen in normal projection, the regions which offers best chance to monitor changes in the fluorescence intensity of the plasma membrane.

Figure 9. a) The hERK1-F64L-S65T-GFP fusion expressed in HEK293 cells treated with 100 mM of the MEK1 inhibitor PD98059 in HAM F-12 (without serum) for 30 minutes at 37 °C. The nuclei empty of fluorescence during this treatment.

b) The same cells as in (a) following treatment with 10 % foetal calf serum for 15 minutes at 37 °C.

c) Time profiles for the redistribution of GFP fluorescence in HEK293 cells following treatment with various concentrations of EGF in Hepes buffer (HAM F-12 replaced with Hepes buffer directly before the experiment). Redistribution of fluorescence is expressed as the change in the ratio value between areas in nucleus and cytoplasm of single cells. Each time profile is the mean for the changes seen in six single cells.

d) Bar chart for the end-point measurements, 600 seconds after start of EGF treatments, of fluorescence change (nucleus:cytoplasm) following various concentrations of EGF.

Figure 10.

a) The SMAD2-EGFP fusion expressed in HEK 293 cells.

b) HEK 293 cells expressing the SMAD2-EGFP fusion were treated with various concentration of TGF-beta as indicated, and the redistribution of fluorescence monitored against time.

The time profile plots represent increases in fluorescence within the nucleus, normalised to starting values in each cell measured. Each trace is the time profile for a single cell nucleus.

- c) A bar chart representing the end-point change in fluorescence within nuclei (after 850 seconds of treatment) for different concentrations of TGF-beta. Each bar is the value for a single nucleus in each treatment.

Figure 11. The VASP-F64L-S65T-GFP fusion in CHO cells stably transfected with the human insulin receptor. The cells were starved for two hours in HAM F-12 without serum, then treated with 10% foetal calf serum. The image shows the resulting redistribution of fluorescence after 15 minutes of treatment. GFP fluorescence becomes localised in structures identified as focal adhesions along the length of actin stress fibres.

Figure 12. Time lapse recording GLUT4-GFP redistribution in CHO-HIR cells. Time indicates minutes after the addition of 100 nM insulin.

- Useful for monitoring the activity of signalling pathways which lead to altered concentrations of cAMP, e.g. activation of G-protein coupled receptors which couple to G-proteins of the G_s or G_i class.

The catalytic subunit of the murine cAMP dependent protein kinase (PKAc) was fused C-terminally to a F64L-S65T derivative of GFP. The resulting fusion (PKAc-F64L-S65T-GFP) was used for monitoring *in vivo* the translocation and thereby the activation of PKA.

15 Convenient restriction endonuclease sites were introduced into the cDNAs encoding murine PKAc (Gen Bank Accession number: M12303) and F64L-S65T-GFP (sequence disclosed in WO 97/11094) by polymerase chain reaction (PCR). The PCR reactions were performed according to standard protocols with the following primers:

20 (SEQ ID NO:3).

5'GFP: TTggACAGAAgCTTTggACAGagCgC GCGT : 3'

455 5'-GATGTTCTTgAgTCTTACTCCgAggTCTTgTATAgTTCATCCATgCCATgT (SEQ ID NO:2).

The PKAc amplification product was then digested with HindIII+Ascl and the F64L-S65T-GFP product with Ascl+XhoI. The two digested PCR products were subsequently ligated with a HindIII+XhoI digested plasmid (pZeoSV® mammalian expression vector, Invitrogen, San Diego, CA, USA). The resulting fusion construct (SEQ ID NO:68 & 69) was under control of the SV40 promoter.

Transfection and cell culture conditions.

Chinese hamster ovary cells (CHO), were transfected with the plasmid containing the PKAc-F64L-S65T-GFP fusion using the calcium phosphate precipitate method in HEPES-buffered saline (Sambrook *et al.*, 1989). Stable transfectants were selected using 1000 mg Zeocin/ml (Invitrogen) in the growth medium (DMEM with 1000 mg glucose/l, 10 % fetal bovine serum (FBS), 100 mg penicillin-streptomycin mixture ml⁻¹, 2 mM L-glutamine purchased from Life Technologies Inc., Gaithersburg, MD, USA). Untransfected CHO cells were used as the control. To assess the effect of glucagon on fusion protein translocation, the PKAc-F64L-S65T-GFP fusion was stably expressed in baby hamster kidney cells overexpressing the human glucagon receptor (BHK/GR cells). Untransfected BHK/GR cells were used as the control. Expression of GR was maintained with 500 mg G418/ml (*Neo* marker) and PKAc-F64L-S65T-GFP was maintained with 500 mg Zeocin/ml (*Sh ble* marker). CHO cells were also simultaneously co-transfected with vectors containing the PKAc-F64L-S65T-GFP fusion and the human $\alpha 2a$ adrenoceptor (hAR $\alpha 2a$).

For fluorescence microscopy, cells were allowed to adhere to Lab-Tek chambered cover-glasses (Nalge Nunc Int., Naperville, IL, USA) for at least 24 hours and cultured to about 80% confluence. Prior to experiments, the cells were cultured over night without selection pressure in HAM F-12 medium with glutamax (Life Technologies), 100 mg penicillin-streptomycin mixture ml⁻¹ and 0.3 % FBS. This medium has low autofluorescence enabling fluorescence microscopy of cells straight from the incubator.

Monitoring activity of PKA with a GFP

The cells were transfected with the PKAc-F64L-S65T-GFP fusion construct and the human $\alpha 2a$ adrenoceptor (hAR $\alpha 2a$) construct. The cells were grown in the presence of Zeocin and G418. For fluorescence microscopy, cells were allowed to adhere to Lab-Tek chambered cover-glasses (Nalge Nunc Int., Naperville, IL, USA) for at least 24 hours and cultured to about 80% confluence. Prior to experiments, the cells were cultured over night without selection pressure in HAM F-12 medium with glutamax (Life Technologies), 100 mg penicillin-streptomycin mixture ml⁻¹ and 0.3 % FBS. This medium has low autofluorescence enabling fluorescence microscopy of cells straight from the incubator.

For fluorescence microscopy, cells were allowed to adhere to Lab-Tek chambered cover-glasses (Nalge Nunc Int., Naperville, IL, USA) for at least 24 hours and cultured to about 80% confluence. Prior to experiments, the cells were cultured over night without selection pressure in HAM F-12 medium with glutamax (Life Technologies), 100 mg penicillin-streptomycin mixture ml⁻¹ and 0.3 % FBS. This medium has low autofluorescence enabling fluorescence microscopy of cells straight from the incubator.

and a 515 ± 15 nm emission filter for minimal image background. The cells were kept and monitored to be at 37°C with a custom built stage heater.

Images were processed and analyzed in the following manner:.

Method 1: Stepwise procedure for quantitation of translocation of PKA:

- 5 1. The image was corrected for dark current by performing a pixel-by-pixel subtraction of a dark image (an image taken under the same conditions as the actual image, except the camera shutter is not allowed to open).
2. The image was corrected for non-uniformity of the illumination by performing a pixel-by-pixel ratio with a flat field correction image (an image taken under the same conditions as the
- 10 actual image of a uniformly fluorescent specimen).
3. The image histogram, i.e., the frequency of occurrence of each intensity value in the image, was calculated.
4. A smoothed, second derivative of the histogram was calculated and the second zero is determined. This zero corresponds to the inflection point of the histogram on the high side of
- 15 the main peak representing the bulk of the image pixel values.
5. The value determined in step 4 was subtracted from the image. All negative values were discarded.
6. The variance (square of the standard deviation) of the remaining pixel values was determined. This value represents the "response" for that image.
- 20 7. Scintillation proximity assay (SPA) for independent quantitation of cAMP:

Method 2: Alternative method for quantitation of PKA redistribution:

1. The fluorescent aggregates are segmented from each image using an automatically
5 found threshold based on the maximisation of the information measure between the object
and background. The *a priori* entropy of the image histogram is used as the information measure.
2. The area of each image occupied by the aggregates is calculated by counting pixels in
the segmented areas.
- 10 3. The value obtained in step 2 for each image in a series, or treatment pair, is normalised to
the value found for the first (unstimulated) image collected. A value of zero (0) indicates no
redistribution of fluorescence from the starting condition. A value of one (1) by this method
equals full redistribution.
- 15 Cells were cultured in HAM F-12 medium as described above, but in 96-well plates. The medium
was exchanged with Ca^{2+} -HEPES buffer including 100 mM IBMX and the cells were
stimulated with different concentrations of forskolin for 10 min. Reactions were stopped with
addition of NaOH to 0.14 M and the amount of cAMP produced was measured with the
cAMP-SPA kit, RPA538 (Amersham) as described by the manufacturer.

20

Manipulating intracellular levels of cAMP to test the PKAc-F64L-S65T-GFP fusion.

The following compounds were used to vary cAMP levels: Forskolin, an activator of adeny-
late cyclase; dbcAMP, a membrane permeable cAMP analog which is not degraded by
phosphodiesterase; IBMX, an inhibitor of phosphodiesterase.

- 25 CHO cells stably expressing the PKAc-F64L-S65T-GFP, showed a dramatic translocation of
the fusion protein to

Fig. 1 shows the response of the cells to 1 mM forskolin (n=4) (Fig. 1) and dbcAMP at 1 mM (n=6).

Fig. 2 shows the progression of response in time following treatment with 1 mM forskolin.

Fig. 3 gives a comparison of the average temporal profiles of fusion protein redistribution and a measure of the extent of each response to the three forskolin concentrations (Fig. 3A, E, B), and to 1 mM dbcAMP (fig 3C) which caused a similar but slower response, and to addition of 100 mM IBMX (n=4, Fig. 3D) which also caused a slow response, even in the absence of adenylate cyclase stimulation. Addition of buffer (n=2) had no effect (data not shown).

As a control for the behavior of the fusion protein, F64L-S65T-GFP alone was expressed in CHO cells and these were also given 50 mM forskolin (n=5); the uniform diffuse distribution characteristic of GFP in these cells was unaffected by such treatment (data not shown).

The forskolin induced translocation of PKAc-F64L-S65T-GFP showed a dose-response relationship (Fig 4 and 6), see quantitative procedures above.

Reversibility of PKAc-F64L-S65T-GFP translocation.

The release of the PKAc probe from its cytoplasmic anchoring hotspots was reversible. Washing the cells repeatedly (5-8 times) with buffer after 10 μ M forskolin treatment completely restored the punctate pattern within 2-5 min (n=2, Fig. 3E). In fact the fusion protein returned to a pattern of fluorescent cytoplasmic aggregates virtually indistinguishable from that observed before forskolin stimulation.

To test whether the return of fusion protein to the cytoplasmic aggregates reflected a decreased [cAMP]_i, cells were treated with a combination of 10 mM forskolin and 100 mM IBMX (n=2) then washed repeatedly (5-8 times) with buffer containing 100 mM IBMX (Fig. 3F). In these experiments, the fusion protein did not return to its prestimulatory localization after removal of forskolin.

Testing the PKA-F64L-S65T-GFP probe with physiologically relevant agents.

To test the probe's response to receptor activation of adenylate cyclase, BHK cells stably

expressed a β -adrenergic receptor coupled to a G α protein which activates adenylate cyclase, thereby increasing the cAMP level. In these cells, addition of 100 nM glucagon (n=2) caused the release of the PKA-F64L-S65T-GFP probe from the cytoplasmic aggregates and a resulting translocation of the fusion protein to a more even cytoplasmic

distribution within 2-3 min (Fig. 3G). Similar but less pronounced effects were seen at lower glucagon concentrations (n=2, data not shown). Addition of buffer (n=2) had no effect over time (data not shown).

Transiently transfected CHO cells expressing hARa2a and the PKA-F64L-S65T-GFP probe
5 were treated with 10 mM forskolin for 7.5 minutes, then, in the continued presence of
forskolin, exposed to 10 mM norepinephrine to stimulate the exogenous adrenoreceptors,
which couple to a G_i protein, which inhibit adenylate cyclase. This treatment led to reappear
ance of fluorescence in the cytoplasmic aggregates indicative of a decrease in [cAMP]_i (Fig.
3H).

10

Fusion protein translocation correlated with [cAMP]_i

As described above, the time it took for a response to come to completion was dependent on
the forskolin dose (Fig. 5) In addition the degree of responses was also dose dependent. To
test the PKA-F64L-S65T-GFP fusion protein translocation in a semi high through-put sy-
15 stem, CHO cells stably transfected with the PKA-F64L-S65T-GFP fusion was stimulated
with buffer and 5 increasing doses of forskolin (n=8). Using the image analysis algorithm de-
scribed above (Method 1), a dose response relationship was observed in the range from
0.01-50 mM forskolin (Fig. 6). A half maximal stimulation was observed at about 2 mM for-
forskolin. In parallel, cells were stimulated with buffer and 8 increasing concentrations of for-
20 skolin (n=4) in the range 0.01-50 mM. The amount of cAMP produced was measured in an
SPA assay. A steep increase was observed between 1 and 5 mM forskolin coincident with
the steepest part of the curve for fusion protein translocation (also Fig. 6)

25 EXAMPLE 2

Real time detection of PKC activity in real time with a GFP probe

Construction of PKC-GFP fusion:

The probe was constructed by ligating two restriction enzyme treated polymerase chain reaction (PCR) amplification products of the cDNA for murine PKC α (GenBank Accession number: M25811) and F64L-S65T-GFP (sequence disclosed in WO 97/11094) respectively. Taq \oplus polymerase and the following oligonucleotide primers were used for PCR;

5' mPKC α : TTggACACAAgCTTTggACACCCTCAggATATggCTgACgTTTACCCggCCAACg (SEQ ID NO:5),

3' mPKC α : gTCATCTTCTCgAgTCTTTCAGgCgCgCCCTACTgCACTTTgCAAgttgggTgC (SEQ ID NO:6),

5' F64L-S65T-GFP: TTggACACAAgCTTTggACACggCgCgCCATgAgTAAggAgAAgAACTT-
10 TTC (SEQ ID NO:1),

3' F64L-S65T-GFP: gTCATCTTCTCgAgTCTTACTCCTgAggTTTgTATAgTTCATCCATgC-CATgT (SEQ ID NO:2).

The hybrid DNA strand was inserted into the pZeoSV \oplus mammalian expression vector as a HindIII-XhoI cassette as described in example 1.

15 Cell Culture:

BHK cells expressing the human M1 receptor under the control of the inducible metallothionine promoter and maintained with the dihydrofolate reductase marker were transfected with the PKC α -F64L-S65T-GFP probe using the calcium phosphate precipitate method in HEPES buffered saline (HBS [pH 7.10]). Stable transfectants were selected using
20 1000 μ g Zeocin \oplus /ml in the growth medium (DMEM with 1000 mg glucose/l, 10 % foetal bovine serum (FBS), 100 mg penicillin-streptomycin mixture ml $^{-1}$, 2 mM L-glutamine). The hM1 receptor and PKC α -F64L-S65T-GFP fusion protein were maintained with 500 nM methotrexate and 500 μ g Zeocin \oplus /ml respectively. 24 hours prior to any experiment, the cells were transferred to HAM F-12 medium with glutamax, 100 μ g penicillin-streptomycin
25 mixture ml $^{-1}$ and 0.3 % FBS. This medium relieves selection pressure, gives a low induction of signal transduction pathways and has a low autofluorescence at the excitation

Monitoring the PKC activity in real time:

Digital images of live cells were gathered using a Zeiss Axiovert 135M fluorescence microscope fitted with a 40X NA 1.30 oil immersion objective and a cooled CCD camera. Images were

CH250 charged coupled device (CCD) camera. The cells were illuminated with a 100 W arc lamp. In the light path was a 470 ± 20 nm excitation filter, a 510 nm dichroic mirror and a 515 ± 15 nm emission filter for minimal image background. The cells were kept and monitored to be at 37°C with a custom built stage heater.

5 Images were analyzed using the IPLab software package for Macintosh.

Upon stimulation of the M1-BHK cells, stably expressing the PKC α -F64L-S65T-GFP fusion, with carbachol we observed a dose-dependent transient translocation from the cytoplasm to the plasma membrane (Fig. 7a,b,c). Simultaneous measurement of the cytosolic free calcium concentration shows that the carbachol-induced calcium mobilisation precedes the translocation (Fig. 8).

Stepwise procedure for quantitation of translocation of PKC:

1. The image was corrected for dark current by performing a pixel-by-pixel subtraction of a dark image (an image taken under the same conditions as the actual image, except the camera shutter is not allowed to open).
2. The image was corrected for non-uniformity of the illumination by performing a pixel-by-pixel ratio with a flat field correction image (an image taken under the same conditions as the actual image of a uniformly fluorescent specimen).
3. A copy of the image was made in which the edges are identified. The edges in the image are found by a standard edge-detection procedure – convolving the image with a kernel which removes any large-scale unchanging components (i.e., background) and accentuates any small-scale changes (i.e., sharp edges). This image was then converted to a binary image by thresholding. Objects in the binary image which are too small to represent the edges of cells were discarded. A dilation of the binary image was performed to close any gaps in the image edges. Any edge objects in the image which were in contact with the borders of the image are discarded. This binary image represents the edge mask.

4. Another copy of image was made via the procedure in step 3. This copy was further

• • • • • 1 •

The original image was masked with the edge mask from step 3 and the sum total of all
30 pixel values is determined.

6. The original image was masked with the whole cell mask from step 4 and the sum total of all pixel values was determined.

7. The value from step 5 was divided by the value from step 6 to give the final result, the fraction of fluorescence intensity in the cells which was localized in the edges.

5

EXAMPLE 3

Probes for detection of mitogen activated protein kinase Erk1 redistribution.

Useful for monitoring signalling pathways involving MAPK, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Erk1, a serine/threonine protein kinase, is a component of a signalling pathway which is activated by e.g. many growth factors.

Probes for detection of ERK-1 activity in real time within living cells:

15 The extracellular signal regulated kinase (ERK-1, a mitogen activated protein kinase, MAPK) is fused N- or C-terminally to a derivative of GFP. The resulting fusions expressed in different mammalian cells are used for monitoring *in vivo* the nuclear translocation, and thereby the activation, of ERK1 in response to stimuli that activate the MAPK pathway.

a) Construction of murine ERK1 - F64L-S65T-GFP fusion:

20 Convenient restriction endonuclease sites are introduced into the cDNAs encoding murine ERK1 (GenBank Accession number: Z14249) and F64L-S65T-GFP (sequence disclosed in WO 97/11094) by polymerase chain reaction (PCR). The PCR reactions are performed according to standard protocols with the following primers:

ERK1-TRACOM

3'ERK1: gTCATCTTCTCgAgTCTTTCAGgCgCgCCCggggCCCTCTggCgCCCCTggCTgg
(SEQ ID NO:8),

5'F64L-S65T-GFP: TTggACACAAgCTTTggACACggCgCgCCATgAgTAAAggAgAAgAACTT-
TTC (SEQ ID NO:1)

- 5 3'F64L-S65T-GFP: gTCATCTTCTCgAgTCTTACTCCTgAggTTTgTATAgTTCATCCATgC-
CATgT (SEQ ID NO:2)

To generate the mERK1-F64L-S65T-GFP (SEQ ID NO:56 & 57) fusion the ERK1 amplifica-
tion product is digested with HindIII+Ascl and the F64L-S65T-GFP product with Ascl+XhoI.
To generate the F64L-S65T-GFP-mERK1 fusion the ERK1 amplification product is then di-
gested with HindIII+Bsu36I and the F64L-S65T-GFP product with Bsu36I+XhoI. The two
10 pairs of digested PCR products are subsequently ligated with a HindIII+XhoI digested plas-
mid (pZeoSV® mammalian expression vector, Invitrogen, San Diego, CA, USA). The resul-
ting fusion constructs are under control of the SV40 promoter.

- 15 b) The human Erk1 gene (GenBank Accession number: X60188) was amplified using PCR
according to standard protocols with primers Erk1-top (SEQ ID NO:9) and Erk1-
bottom/+stop (SEQ ID NO:10). The PCR product was digested with restriction enzymes E-
coR1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession
number U55763) digested with EcoR1 and BamH1. This produces an EGFP-Erk1 fusion
20 (SEQ ID NO:38 & 39) under the control of a CMV promoter.

The plasmid containing the EGFP-Erk1 fusion was transfected into HEK293 cells employing
the FUGENE transfection reagent (Boehringer Mannheim). Prior to experiments the cells
were grown to 80%-90% confluency 8 well chambers in DMEM with 10% FCS. The cells we-
25 re washed in plain HAM F-12 medium (without FCS), and then incubated for 30-60 minutes
in plain HAM F-12 (without FCS) with 100 micromolar PD98059, an inhibitor of MEK1, a ki-
nase which activates Erk1; this step effectively inactivates Erk1.

For experiments where the mek1 inhibitor or blocking of MEK1 is still wanted
(e.g. in control experiments), the inhibitor is included in the HEPES buffer.

The experimental setup of the microscope was as described in example 1.

60 images were collected with 10 seconds between each, and with the test compound added after image number 10.

5 Addition of EGF (1-100 nM) caused within minutes a redistribution of EGFP-Erk1 from the cytoplasm into the nucleus (Fig. 9a,b).

The response was quantitated as described below and a dose-dependent relationship between EGF concentration and nuclear translocation of EGFP-Erk1 was found (Fig. 9c,d). Redistribution of GFP fluorescence is expressed in this example as the change in the ratio value between areas in nuclear versus cytoplasmic compartments of the cell. Each time profile is
10 the average of nuclear to cytoplasmic ratios from six cells in each treatment.

EXAMPLE 4:

Probes for detection of Erk2 redistribution.

Useful for monitoring signalling pathways involving MAPK, e.g. to identify compounds which
15 modulate the activity of the pathway in living cells.

Erk2, a serine/threonine protein kinase, is closely related to Erk1 but not identical; it is a component of a signalling pathway which is activated by e.g. many growth factors.

a) The rat Erk2 gene (GenBank Accession number: M64300) was amplified using PCR according to standard protocols with primers Erk2-top (SEQ ID NO:11) and Erk2-bottom/+stop
20 (SEQ ID NO:13) The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an EGFP-Erk2 fusion (SEQ ID NO:40 &41) under the control of a CMV promoter.

25 b) The rat Erk2 gene (GenBank Accession number: M64300) was amplified using PCR according to standard protocols with primers (SEQ ID NO:11 &12).

c) The rat Erk2 gene (GenBank Accession number: M64300) was amplified using PCR according to standard protocols with primers (SEQ ID NO:11 &12). The PCR product was digested with Xho1 and BamH1. This produces an Erk2-EGFP fusion (SEQ ID NO:58 &59) under
30 the control of a CMV promoter.

The resulting plasmids were transfected into CHO cells and BHK cells. The cells were grown under standard conditions. Prior to experiments, the cells were starved in medium without serum for 48-72 hours. This led to a predominantly cytoplasmic localization of both probes, especially in BHK cells. 10% fetal calf serum was added to the cells and the fluorescence of the cells was recorded as explained in example 3. Addition of serum caused the probes to redistribute into the nucleus within minutes of addition of serum.

EXAMPLE 5:

10 Probes for detection of Smad2 redistribution.

Useful for monitoring signalling pathways activated by some members of the transforming growth factor-beta family, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Smad 2, a signal transducer, is a component of a signalling pathway which is induced by some members of the TGFbeta family of cytokines.

a) The human Smad2 gene (GenBank Accession number: AF027964) was amplified using PCR according to standard protocols with primers Smad2-top (SEQ ID NO:24) and Smad2-bottom/+stop (SEQ ID NO:26) . The PCR product was digested with restriction enzymes EcoR1 and Acc65I, and ligated into pEGFP-C1 (Clontech; Palo Alto; GenBank Accession number U55763) digested with EcoR1 and Acc65I. This produces an EGFP-Smad2 fusion (SEQ ID NO:50&51) under the control of a CMV promoter.

b) The human Smad2 gene (GenBank Accession number: AF027964) was amplified using PCR according to standard protocols with primers Smad2-top (SEQ ID NO:24) and Smad2-bottom/-stop (SEQ ID NO:25) . The PCR product was digested with restriction enzymes EcoR1 and Acc65I, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and Acc65I.

30 The plasmid containing the EGFP-Smad2 fusion was transfected into HEK293 cells, where it showed a cytoplasmic distribution. Prior to experiments the cells were grown in the presence of

chambers in DMEM with 10% FCS to 80% confluency and starved overnight in HAM F-12 medium without FCS.

For experiments, the HAM F-12 medium was replaced with Hepes buffer pH 7.2.

The experimental setup of the microscope was as described in example 1.

- 5 90 images were collected with 10 seconds between each, and with the test compound added after image number 5.

After serum starvation of cells, each nucleus contains less GFP fluorescence than the surrounding cytoplasm (Fig. 10a). Addition of TGFbeta caused within minutes a redistribution of EGFP-Smad2 from the cytoplasm into the nucleus (Fig. 10b).

The redistribution of fluorescence within the treated cells was quantified simply as the fractional increase in nuclear fluorescence normalised to the starting value of GFP fluorescence in the nucleus of each unstimulated cell.

15 **EXAMPLE 6:**

Probe for detection of VASP redistribution.

Useful for monitoring signalling pathways involving rearrangement of cytoskeletal elements, e.g. to identify compounds which modulate the activity of the pathway in living cells.

VASP, a phosphoprotein, is a component of cytoskeletal structures, which redistributes in response to signals which affect focal adhesions.

- 20 a) The human VASP gene (GenBank Accession number: Z46389) was amplified using PCR according to standard protocols with primers VASP-top (SEQ ID NO:94) and VASP-bottom/+stop (SEQ ID NO:95). The PCR product was digested with restriction enzymes Hind3 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Hind3 and BamH1. This produces an EGFP-VASP fusion (SEQ ID NO:124 & 125) under the

control of the CMV promoter. Cells expressing the human insulin receptor were transfected using the calcium-phosphate tranfection method. Prior to experiments, cells were grown in 8 well Nunc chambers and starved overnight in medium without FCS.

Experiments are performed in a microscope setup as described in example 1.

10% FCS was added to the cells and images were collected. The EGFP-VASP fusion was redistributed from a somewhat even distribution near the periphery into more localized structures, identified as focal adhesion points (Fig. 11).

5

A large number of further GFP fusions have been made or are in the process of being made, as apparent from the following Examples 7-22 which also suggest suitable host cells and substances for activation of the cellular signalling pathways to be monitored and analyzed.

10

EXAMPLE 7:

Probe for detection of actin redistribution.

- 15 Useful for monitoring signalling pathways involving rearrangement or formation of actin filaments, e.g. to identify compounds which modulate the activity of pathways leading to cytoskeletal rearrangements in living cells.

Actin is a component of cytoskeletal structures, which redistributes in response to very many cellular signals.

20

The actin binding domain of the human alpha-actinin gene (GenBank Accession number: X15804) was amplified using PCR according to standard protocols with primers ABD-top (SEQ ID NO:90) and ABD-bottom/-stop (SEQ ID NO:91). The PCR product was digested with restriction enzymes Hind3 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto;

- 25 GenBank Accession number U55762) digested with Hind3 and BamH1. This construct encodes an actin binding domain fused to the C-terminus of the enhanced green fluorescent protein (EGFP).

The resulting plasmid was transfected into CHO cells expressing the human insulin receptor. Cells were stimulated with insulin which caused the actin binding domain-EGFP probe to become redistributed into morphologically distinct membrane-associated structures.

30

Example 8:

Probes for detection of p38 redistribution.

- 5 Useful for monitoring signalling pathways responding to various cellular stress situations, e.g. to identify compounds which modulate the activity of the pathway in living cells, or as a counterscreen.

p38, a serine/threonine protein kinase, is a component of a stress-induced signalling pathway which is activated by many types of cellular stress, e.g. TNFalpha, anisomycin, UV and mitomycin C.

10

a) The human p38 gene (GenBank Accession number: L35253) was amplified using PCR according to standard protocols with primers p38-top (SEQ ID NO:14) and p38-bottom/+stop (SEQ ID NO: 16). The PCR product was digested with restriction enzymes

15 Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produced an EGFP-p38 fusion (SEQ ID NO:46 &47) under the control of a CMV promoter.

b) The human p38 gene (GenBank Accession number: L35253) was amplified using PCR according to standard protocols with primers p38-top (SEQ ID NO:13) and p38-bottom/-stop (SEQ ID NO:15). The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number

20 U55762) digested with Xho1 and BamH1. This produced a p38-EGFP fusion (SEQ ID NO:64 &65) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. HEK293, in which the

25 EGFP-p38 probe and/or the p38-EGFP probe should change its cellular distribution from predominantly cytoplasmic to nuclear within minutes in response to activation of the signalling pathway with a suitable agent.

Example 9:

30 Probes for detection of Jnk1 redistribution.

Useful for monitoring signalling pathways responding to various cellular stress situations, e.g. to identify compounds which modulate the activity of the pathway in living cells, or as a counterscreen.

Jnk1, a serine/threonine protein kinase, is a component of a stress-induced signalling pathway different from the p38 described above, though it also is activated by many types of cellular stress, e.g. TNFalpha, anisomycin and UV.

a) The human Jnk1 gene (GenBank Accession number: L26318) was amplified using PCR according to standard protocols with primers Jnk-top (SEQ ID NO:17) and Jnk-bottom/+stop (SEQ ID NO:19). The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produced an EGFP-Jnk1 fusion (SEQ ID NO:44 &45) under the control of a CMV promoter.

b) The human Jnk1 gene (GenBank Accession number: L26318) was amplified using PCR according to standard protocols with primers Jnk-top (SEQ ID NO:17) and Jnk-bottom/-stop (SEQ ID NO:18). The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produced a Jnk1-EGFP fusion (SEQ ID NO:62 &63) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. HEK293, in which the EGFP-Jnk1 probe and/or the Jnk1-EGFP probe should change its cellular distribution from predominantly cytoplasmic to nuclear in response to activation of the signalling pathway with e.g. anisomycin.

25

Example 10:

Probes for detection of PKG activation

analogues of cGMP levels

Identify compounds which modulate the activity of the pathway in living cells.

PGK, a cGMP-dependent serine/threonine protein kinase, mediates the guanylyl-cyclase/cGMP signal

a) The human PKG gene (GenBank Accession number: Y07512) is amplified using PCR according to standard protocols with primers PKG-top (SEQ ID NO:81) and PKG-bottom/+stop (SEQ ID NO:83). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an EGFP-PKG fusion (SEQ ID NO:134 &135) under the control of a CMV promoter.

b) The human PKG gene (GenBank Accession number: Y07512) is amplified using PCR according to standard protocols with primers PKG-top (SEQ ID NO:81) and PKG-bottom/-stop (SEQ ID NO: 82). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produces a PKG-EGFP fusion (SEQ ID NO:136 &137) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. A10, in which the EGFP-PKG probe and/or the PKG-EGFP probe should change its cellular distribution from cytoplasmic to one associated with cytoskeletal elements within minutes in response to treatment with agents which raise nitric oxide (NO) levels.

Example 11:

Probes for detection of IkappaB kinase redistribution.

Useful for monitoring signalling pathways leading to NFkappaB activation, e.g. to identify compounds which modulate the activity of the pathway in living cells.

IkappaB kinase, a serine/threonine kinase, is a component of a signalling pathway which is activated by a variety of inducers including cytokines, lymphokines, growth factors and stress.

a) The alpha subunit of IkappaB kinase (GenBank Accession number U55763) is amplified using PCR according to standard protocols with primers IKK-top (SEQ ID NO:96) and IKK-bottom/+stop (SEQ ID NO:98). The PCR product is digested with restriction enzymes EcoR1 and Acc65I, and ligated into pEGFP-C1 (Clontech, Palo Alto;

GenBank Accession number U55763) digested with EcoR1 and Acc65I. This produces an EGFP-IkappaB-kinase fusion (SEQ ID NO:120 &121) under the control of a CMV promoter.

- b) The alpha subunit of the human IkappaB kinase gene (GenBank Accession number: AF009225) is amplified using PCR according to standard protocols with primers IKK-top (SEQ ID NO:96) and IKK-bottom/-stop (SEQ ID NO:97). The PCR product is digested with restriction enzymes EcoR1 and Acc65I, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and Acc65I. This produces an IkappaB-kinase-EGFP fusion (SEQ ID NO:122 &123) under the control of a CMV promoter.

- The resulting plasmids are transfected into a suitable cell line, e.g. Jurkat, in which the EGFP-IkappaB-kinase probe and/or the IkappaB-kinase-EGFP probe should achieve a more cytoplasmic distribution within seconds following stimulation with e.g. TNFalpha.

Example 12:

Probes for detection of CDK2 redistribution.

- Useful for monitoring signalling pathways of the cell cycle, e.g. to identify compounds which modulate the activity of the pathway in living cells.

CDK2, a cyclin-dependent serine/threonine kinase, is a component of the signalling system which regulates the cell cycle.

- a) The human CDK2 gene (GenBank Accession number: X61622) is amplified using PCR according to standard protocols with primers CDK2-top (SEQ ID NO:102) and CDK2-bottom/+stop (SEQ ID NO: 104). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an EGFP-CDK2 fusion (SEQ ID NO:114 &115) under the control of a CMV promoter.

b) The human CDK2 gene (GenBank Accession number: X61622) is amplified according to standard protocols with primers CDK2-top (SEQ ID NO:102) and CDK2-bottom/+stop (SEQ ID NO:104). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produces a CDK2-EGFP fusion (SEQ ID NO:112 &113) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. HEK293 in which the EGFP-CDK2 probe and/or the CDK2-EGFP probe should change its cellular distribution from cytoplasmic in contact-inhibited cells, to nuclear location in response to activation with a number of growth factors, e.g. IGF.

5

Example 13:

Probes for detection of Grk5 redistribution.

Useful for monitoring signalling pathways involving desensitization of G-protein coupled receptors, e.g. to identify compounds which modulate the activity of the pathway in living cells.

- 10 Grk5, a G-protein coupled receptor kinase, is a component of signalling pathways involving membrane bound G-protein coupled receptors.

- a) The human Grk5 gene (GenBank Accession number: L15388) is amplified using PCR according to standard protocols with primers Grk5-top (SEQ ID NO:27) and Grk5-
15 bottom/+stop (SEQ ID NO:29). The PCR product is digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with EcoR1 and BamH1. This produces an EGFP-Grk5 fusion (SEQ ID NO:42 &43) under the control of a CMV promoter.

- b) The human Grk5 gene (GenBank Accession number: L15388) is amplified using PCR according to standard protocols with primers Grk5-top (SEQ ID NO:27) and Grk5-bottom/-stop (SEQ ID NO:28). The PCR product is digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and BamH1. This produces a Grk5-EGFP fusion (SEQ ID NO:60 &61) under the control of a CMV promoter.

- 25 The resulting plasmids are transfected into a suitable cell line, e.g. HEK293 expressing a rat dopamine D1A receptor, in which the EGFP-Grk5 probe and/or the Grk5-EGFP probe should change its cellular distribution.

- 30 Example 14:

Probes for detection of Zap70 redistribution.

Useful for monitoring signalling pathways involving the T cell receptor, e.g. to identify compounds which modulate the activity of the pathway in living cells.

5 Zap70, a tyrosine kinase, is a component of a signalling pathway which is active in e.g. T-cell differentiation.

a) The human Zap70 gene (GenBank Accession number: L05148) is amplified using PCR according to standard protocols with primers Zap70-top (SEQ ID NO:105) and Zap70-bottom/+stop (SEQ ID NO:107). The PCR product is digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-C1 (GenBank Accession number U55763) digested with EcoR1 and BamH1. This produces an EGFP-Zap70 fusion (SEQ ID NO:108 &109) under the control of a CMV promoter.

15 b) The human Zap70 gene (GenBank Accession number: L05148) is amplified using PCR according to standard protocols with primers Zap70-top (SEQ ID NO:105) and Zap70-bottom/-stop (SEQ ID NO:106). The PCR product is digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and BamH1. This produces a Zap70-EGFP fusion (SEQ ID NO:110 &111) under the control of a CMV promoter.

20 The resulting plasmids are transfected into a suitable cell line, e.g. Jurkat, in which the EGFP-Zap70 probe and/or the Zap70-EGFP probe should change its cellular distribution from cytoplasmic to membrane-associated within seconds in response to activation of the T cell receptor signalling pathway with e.g. antibodies to CD3epsilon.

Example 15:

25 Probes for detection of p85 redistribution.

Useful for monitoring signalling pathways involving PI-3 kinase, e.g. to identify compounds which modulate the activity of the pathway in living cells.

p85 is a component of many pathways involving membrane-bound tyrosine kinase receptors and G-protein-coupled receptors.

a) The human p85alpha gene (GenBank Accession number: M61906) was amplified using PCR according to standard protocols with primers p85-top-C (SEQ ID NO:22) and p85-bottom/+stop (SEQ ID NO:23). The PCR product was digested with restriction enzymes Bgl2 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Bgl2 and BamH1. This produced an EGFP-p85alpha fusion (SEQ ID NO:48 &49) under the control of a CMV promoter.

b) The human p85alpha gene (GenBank Accession number: M61906) was amplified using PCR according to standard protocols with primers p85-top-N (SEQ ID NO:20) and p85-bottom/-stop (SEQ ID NO:21). The PCR product was digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and BamH1. This produced a p85alpha-EGFP fusion (SEQ ID NO:66 &67) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. CHO expressing the human insulin receptor, in which the EGFP-p85 probe and/or the p85-EGFP probe may change its cellular distribution from cytoplasmic to membrane-associated within minutes in response to activation of the receptor with insulin.

Example 16:

Probes for detection of protein-tyrosine phosphatase redistribution.

Useful for monitoring signalling pathways involving tyrosine kinases, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Protein-tyrosine phosphatase1C, a tyrosine-specific phosphatase, is an inhibitory component in signalling pathways involving e.g. some growth factors.

a) The human protein-tyrosine phosphatase 1C gene (GenBank Accession number: X62055) is amplified using PCR according to standard protocols with primers PTP-top (SEQ ID NO:99) and PTP-bottom/+stop (SEQ ID NO:100). The PCR product is digested with XhoI and EcoRI. This produces an EGFP-PTP fusion (SEQ ID NO:116 &117) under the control of a CMV promoter.

- b) The human protein-tyrosine phosphatase 1C gene (GenBank Accession number: X62055) is amplified using PCR according to standard protocols with primers PTP-top (SEQ ID NO:99) and PTP-bottom/-stop (SEQ ID NO:100). The PCR product is digested with restriction enzymes Xho1 and EcoR1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and EcoR1. This produces a PTP-EGFP fusion (SEQ ID NO:118 & 119) under the control of a CMV promoter.
- The resulting plasmids are transfected into a suitable cell line, e.g. MCF-7 in which the EGFP-PTP probe and/or the PTP-EGFP probe should change its cellular distribution from cytoplasm to the plasma membrane within minutes in response to activation of the growth inhibitory signalling pathway with e.g. somatostatin.

Example 17:

Probes for detection of Smad4 redistribution.

- Useful for monitoring signalling pathways involving most members of the transforming growth factor-beta family, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Smad4, a signal transducer, is a common component of signalling pathways induced by various members of the TGFbeta family of cytokines.

- a) The human Smad4 gene (GenBank Accession number: U44378) was amplified using PCR according to standard protocols with primers Smad4-top and Smad4-bottom/+stop (SEQ ID NO:35). The PCR product was digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with EcoR1 and BamH1. This produce an EGFP-Smad4 fusion (SEQ ID NO:52 & 53) under the control of a CMV promoter.
- b) The human Smad4 gene (GenBank Accession number: U44378) was amplified using PCR according to standard protocols with primers Smad4-top and Smad4-bottom/+stop (SEQ ID NO:35). The PCR product was digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and BamH1. This produced a Smad4-EGFP fusion (SEQ ID NO:76 & 77) under the control of a CMV promoter.

The resulting plasmids are transfected into a cell line, e.g. HEK293 in which the EGFP-Smad4 probe and/or the Smad4-EGFP probe should change its cellular distribution within minutes from cytoplasmic to nuclear in response to activation of the signalling pathway with e.g. TGFbeta.

5

Example 18:

Probes for detection of Stat5 redistribution.

Useful for monitoring signalling pathways involving the activation of tyrosine kinases of the Jak family, e.g. to identify compounds which modulate the activity of the pathway in living

10

cells.

Stat5, signal transducer and activator of transcription, is a component of signalling pathways which are induced by e.g. many cytokines and growth factors.

15

a) The human Stat5 gene (GenBank Accession number: L41142) was amplified using PCR according to standard protocols with primers Stat5-top (SEQ ID NO:30) and Stat5-bottom/+stop (SEQ ID NO:32). The PCR product was digested with restriction enzymes Bgl2 and Acc65I, and ligated into pEGFP-C1 (Clontech; Palo Alto; GenBank Accession number U55763) digested with Bgl2 and Acc65I. This produced an EGFP-Stat5 fusion (SEQ ID NO:54 &55) under the control of a CMV promoter.

20

b) The human Stat5 gene (GenBank Accession number: L41142) was amplified using PCR according to standard protocols with primers Stat5-top (SEQ ID NO:30) and Stat5-bottom/-stop (SEQ ID NO:331). The PCR product was digested with restriction enzymes Bgl2 and Acc65I, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Bgl2 and Acc65I. This produced a Stat5-EGFP fusion (SEQ ID NO:78 &79) under the control of a CMV promoter.

25

The resulting plasmids are transfected into a suitable cell line, e.g. MIN6 in which the EGFP-Stat5 probe and/or the Stat5-EGFP probe should change its cellular distribution within minutes from cytoplasmic to nuclear in response to activation of the signalling pathway with e.g. TGFbeta.

30

Example 19:

Probes for detection of NFAT redistribution.

Useful for monitoring signalling pathways involving activation of NFAT, e.g. to identify compounds which modulate the activity of the pathway in living cells.

- 5 NFAT, an activator of transcription, is a component of signalling pathways which is involved in e.g. immune responses.
- a) The human NFAT1 gene (GenBank Accession number: U43342) is amplified using PCR according to standard protocols with primers NFAT-top (SEQ ID NO:84) and NFAT-bottom/+stop (SEQ ID NO:86). The PCR product is digested with restriction enzymes Xho1 and EcoR1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and EcoR1. This produces an EGFP-NFAT fusion (SEQ ID NO:130 &131) under the control of a CMV promoter.
- 10 b) The human NFAT gene (GenBank Accession number: U43342) is amplified using PCR according to standard protocols with primers NFAT-top (SEQ ID NO:84) and NFAT-bottom/-stop (SEQ ID NO:85). The PCR product is digested with restriction enzymes Xho1 and EcoR1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and EcoR1. This produces an NFAT-EGFP fusion (SEQ ID NO:132 &133) under the control of a CMV promoter.
- 15
- 20 The resulting plasmids are transfected into a suitable cell line, e.g. Jurkat, in which the EGFP-NFAT probe and/or the NFAT-EGFP probe should change its cellular distribution from cytoplasmic to nuclear within minutes in response to activation of the signalling pathway with e.g. antibodies to CD3epsilon.

25 Example 20:

Probes for detection of NFkappaB redistribution

NFkappaB, an activator of transcription, is a component of signalling pathways which are responsive to a variety of inducers including cytokines, lymphokines, some immunosuppressive agents.

- 5 a) The human NFkappaB p65 subunit gene (GenBank Accession number: M62399) is amplified using PCR according to standard protocols with primers NFkappaB-top (SEQ ID NO:87) and NFkappaB-bottom/+stop (SEQ ID NO:89). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an
10 EGFP-NFkappaB fusion (SEQ ID NO:142 & 143) under the control of a CMV promoter.

- b) The human NFkappaB p65 subunit gene (GenBank Accession number: M62399) is amplified using PCR according to standard protocols with primers NFkappaB-top (SEQ ID NO:87) and NFkappaB-bottom/-stop (SEQ ID NO:88). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produces an
15 NFkappaB-EGFP fusion (SEQ ID NO:140 & 141) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. Jurkat, in which the EGFP-NFkappaB probe and/or the NFkappaB-EGFP probe should change its cellular distribution from cytoplasmic to nuclear in response to activation of the signalling pathway with
20 e.g. TNFalpha.

Example 21:

Probe for detection of RhoA redistribution.

- Useful for monitoring signalling pathways involving RhoA, e.g. to identify compounds which
25 modulate the activity of the pathway in living cells.

RhoA, a small GTPase, is a component of many signalling pathways, e.g. FAK and skeletal rearrangement.

- The human RhoA gene (GenBank Accession number: L25080) was amplified using PCR
30 according to standard protocols with primers RhoA-top (SEQ ID NO:92) and RhoA-bottom/+stop (SEQ ID NO:93). The PCR product was digested with restriction enzymes

Hind3 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Hind3 and BamH1. This produced an EGFP-RhoA fusion (SEQ ID NO:126 & 127) under the control of a CMV promoter.

The resulting plasmid is transfected into a suitable cell line, e.g. Swiss3T3, in which the EGFP-RhoA probe should change its cellular distribution from a reasonably homogenous to a peripheral distribution within minutes of activation of the signalling pathway with e.g. LPA.

Example 22:

Probes for detection of PKB redistribution.

Useful for monitoring signalling pathways involving PKB e.g. to identify compounds which modulate the activity of the pathway in living cells.

PKB, a serine/threonine kinase, is a component in various signalling pathways, many of which are activated by growth factors.

a) The human PKB gene (GenBank Accession number: M63167) is amplified using PCR according to standard protocols with primers PKB-top (SEQ ID NO:36) and PKB-bottom/+stop (SEQ ID NO:80). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an EGFP-PKB fusion (SEQ ID NO:138 & 139) under the control of a CMV promoter.

b) The human PKB gene (GenBank Accession number: M63167) was amplified using PCR according to standard protocols with primers PKB-top (SEQ ID NO:36) and PKB-bottom/-stop (SEQ ID NO:37). The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produced a PKB-EGFP fusion (SEQ ID NO:70 & 71) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. CHO expressing the human insulin receptor.

The cells are grown in the presence of insulin. Upon addition of insulin, the transition should be apparent within minutes.

REFERENCES:

- Adams, S.R., Harootunian, A.T., Buechler, Y.J., Taylor, S.S. & Tsien, R.Y. (1991) *Nature* **349**, 694-697
- 5 Blobe, G.C., Stribling, D.S., Fabbro, D., Stabel, S & Hannun, Y.A. (1996) *J. Biol. Chem.* **271**, 15823-15830
- Chalfie, M., Tu, Y., Euskirchen, G., Ward, W.W. & Prasher, D.C. (1994) *Science* **263**, 802-805
- Cossette, L.J., Hoglinger, O., Mou, L.J. & Shen, S.H. (1997) *Exp. Cell Res.* **223**, 459-466
- 10 DeBernardi, M.A. & Brooker, G. (1996) *Proc. Natl. Acad. Sci. USA* **93**, 4577-4582
- Farese, R.V.. (1992) *Biochem. J.* **288**, 319-323
- Fulop Jr., T., Leblanc, C., Lacombe, G. & Dupuis, G. (1995) *FEBS Lett.* **375**, 69-74
- Godson, C., Masliah, E., Balboa, M.A., Ellisman, M.H. & Insel, P.A. (1996) *Biochem. Biophys. Acta* **1313**, 63-71
- 15 Khalil, R.A., Lajoie, C., Resnick, M.S. & Morgan, K.G. (1992) *American Physiol. Society c*, 714-719
- Sano, M., Kohno, M. & Iwanaga, M. (1995) *Brain Res.* **688**, 213-218
- Bastiaens, P.I.H. & Jovin, T.M. (1996) *Proc. Natl. Acad. Sci. USA* **93**, 8407-8412
- Schmidt, D.J., Ikebe, M., Kitamura, K., & Fay, F.S. (1997) *FASEB J.* **11**, 2924 (Abstract)
- 20 Sakai, N., Sasaki, K., Hasegawa, C., Ohkura, M., Suminka, K., Shirai, Y. & Saito, N. (1996) *Soc. Neuroscience* **22**, 69P (Abstract)
- Sakai, N., Sakai, K., Hasegawa, C., Ohkura, M., Sumioka, ., Shirai, Y., & Naoaki, S. (1997) *Japanese Journal of Pharmacology* **73**, 69P (Abstract of a meeting held 22-23 March)

SEQUENCE LISTING

5 (1) GENERAL INFORMATION

- (i) APPLICANT: NovoNordisk, BioImage
- 10 (ii) TITLE OF THE INVENTION: A Method of Detecting Cellular
Translocation of Biologically Active Polypeptides Using
Fluorescence Imaging
- (iii) NUMBER OF SEQUENCES: 143
- 15 (iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: NovoNordisk, BioImage
(B) STREET: Mørkhøjbygade 28
(C) CITY: Søborg
(D) STATE: DK
20 (E) COUNTRY: DENMARK
(F) ZIP: 2860
- (v) COMPUTER READABLE FORM:
25 (A) MEDIUM TYPE: Diskette
(B) COMPUTER: IBM Compatible
(C) OPERATING SYSTEM: DOS
(D) SOFTWARE: FastSEQ for Windows Version 2.0
- 30 (viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: , PV&P R
(B) REGISTRATION NUMBER:
(C) REFERENCE/DOCKET NUMBER:

35 (2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:
- 40 (A) LENGTH: 53 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

TTGGACACAA GCTTTGGACA CGGCGGCCA TGAGTAAAGG AGAAGAACTT TTC

- 55 (A) LENGTH: 53 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

5 GTCATCTTCT CGAGTCTTAC TCCTGAGGTT TGTATAGTTC ATCCATGCCA TGT 53

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

- 10 (A) LENGTH: 54 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

TTGGACACAA GCTTTGGACA CCCTCAGGAT ATGGGCAACG CCGCCGCCGC CAAG 54

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

- 20 (A) LENGTH: 55 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
25 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

30 GTCATCTTCT CGAGTCTTTC AGGCGCGCCC AAACCTCAGTA AACTCCTTGC CACAC 55

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

- 35 (A) LENGTH: 55 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

TTGGACACAA GCTTTGGACA CCCTCAGGAT ATGGCTGACG TTTACCCGGC CAACG 55

45

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 55 base pairs

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

GTCATCTTCT CGAGTCTTTC AGGCGCGCCC AAACCTCAGTA AACTCCTTGC CACAC

(2) INFORMATION FOR SEQ ID NO:7:

- 5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 64 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

15 TTGGACACAA GCTTTGGACA CCCTCAGGAT ATGGCGCGCGG CGGCGGCGGC TCCGGGGGGC 60
GGGG 64

(2) INFORMATION FOR SEQ ID NO:8:

- 20 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 55 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

GTCACTCTCT CGAGTCTTTC AGGCGCGCCC GGGGCCCTCT GGCGCCCTG GCTGG 55

30

(2) INFORMATION FOR SEQ ID NO:9:

- 35 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

40 TAGAATTCAA CCATGGCGGC GGCGCGGCG

(2) INFORMATION FOR SEQ ID NO:10:

30

- 45 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

55

AGAGGCGCTC CAGCACTCC

(2) INFORMATION FOR SEQ ID NO:11:

29

60

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
5 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

10 TACTCGAGTA ACCATGGCGG CGGCGGCGGC G 31

(2) INFORMATION FOR SEQ ID NO:12:

- (i) SEQUENCE CHARACTERISTICS:
15 (A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

TAGGATCCAT AGATCTGTAT CCTGG 25

25 (2) INFORMATION FOR SEQ ID NO:13:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 base pairs
(B) TYPE: nucleic acid
30 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

35 TAGGATCCTT AAGATCTGTA TCCTGG 26

(2) INFORMATION FOR SEQ ID NO:14:

- (i) SEQUENCE CHARACTERISTICS:
40 (A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

- SEQUENCE CHARACTERISTICS:
55 (A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

61

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

5

ATGGATCCTC GGACTCCATC TCTTCTTG

28

(2) INFORMATION FOR SEQ ID NO:16:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 29 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

ATGGATCCTC AGGACTCCAT CTCTTCTTG

29

20

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 28 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

25

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

GTCTCGAGCC ATCATGAGCA GAAGCAAG

28

35

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

GTGGATCCCA CTGCTGCACC TGTGCTA

27

45

(2) INFORMATION FOR SEQ ID NO:19:

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

GTGGATCCTC ACTGCTGCAC CTGTGCTA

28

(2) INFORMATION FOR SEQ ID NO:20:

5

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 40 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

10

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

15

CGCGAATTCC GCCACCATGA GTGCTGAGGG GTACCACTAC

40

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:

20

(A) LENGTH: 32 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

CGCGGATCCT GTCGCCTCTG CTGTGCATAT AC

32

30

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 30 base pairs

(B) TYPE: nucleic acid

35

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(vi) ORIGINAL SOURCE:

(A) ORGANISM: p85-top-C

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

GGGAGATCTA TGAGTGCTGA GGGGTACCAG

30

45

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 30 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

55

CGCGGATCCT GTCGCCTCTG CTGTGCATAT AC

(2) INFORMATION FOR SEQ ID NO:24:

- 5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 33 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

GTGAATTCGA CCATGTCGTC CATCTTGCCA TTC

15

(2) INFORMATION FOR SEQ ID NO:25:

33

- 20 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

GTGGTACCCA TGACATGCTT GAGCAACGCA C

(2) INFORMATION FOR SEQ ID NO:26:

31

30

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

40 GTGGTACCTT ATGACATGCT TGAGCAACGC AC

(2) INFORMATION FOR SEQ ID NO:27:

32

45

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

55

(2) INFORMATION FOR SEQ ID NO:28:

31

- (i) SEQUENCE CHARACTERISTICS:

64

- (A) LENGTH: 30 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

GTGGATCCCT GCTGCTTCCG GTGGAGTTTCG 30

10

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 31 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

15

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

GTGGATCCCT AGCTGCTTCC GGTGGAGTTC G 31

25

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 32 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

GTAGATCTAC CATGGCGGGC TGGATCCAGG CC 32

35

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 31 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

40

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

GTGGTACCCA TGAGAGGGAG CCTCTGGGAC

55

- (A) LENGTH: 31 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

5 GTGGTACCTC ATGAGAGGGA GCCTCTGGCA G 31

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:

- 10 (A) LENGTH: 33 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

GTGAATTCAA CCATGGACAA TATGTCTATT ACG 33

20 (2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
25 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

GTGGATCCCA GTCTAAAGGT TGTGGGTCTG C 31

(2) INFORMATION FOR SEQ ID NO:35:

35 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
40 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

45 GTGGATCCTC AGTCTAAAGG TTGTGGGTCT GC 32

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

66

GTCTCGAGGC ACCATGAGCG ACGTGGC

27

(2) INFORMATION FOR SEQ ID NO:37:

- 5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 27 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 10 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

TGGGATCCGA GGCCGTGCTG CTGGCCG

27

(2) INFORMATION FOR SEQ ID NO:38:

- 15 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1896 base pairs
 20 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 25 (ii) MOLECULE TYPE: cDNA
 (ix) FEATURE:
 (A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...1891
 30 (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG	48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu	
1 5 10 15	
GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC	96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly	
20 25 30	
GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC	144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile	
35 40 45	
TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC	192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr	
50 55 60	

CTG ACC TAC GGC

CTG ACC TAC GGC AAG TCC GGC ATG CCC GAA GGC TAC GTC CAG GAG	288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu	
85 90	

67

	CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG	336
	Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu	
	100 105 110	
5	GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC	384
	Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly	
	115 120 125	
10	ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC	432
	Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr	
	130 135 140	
15	AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC	480
	Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn	
	145 150 155 160	
20	GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC	528
	Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser	
	165 170 175	
25	GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC	576
	Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly	
	180 185 190	
30	CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG	624
	Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu	
	195 200 205	
35	AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC	672
	Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe	
	210 215 220	
40	GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC	720
	Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser	
	225 230 235 240	
45	GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCA ACC ATG GCG GCG GCG	768
	Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Ala Ala Ala	
	245 250 255	
50	GCG GCT CAG GGG GGC GGG GGC GGG GAG CCC CGT AGA ACC GAG GGG GTC	816
	Ala Ala Gln Gly Gly Gly Gly Gly Glu Pro Arg Arg Thr Glu Gly Val	
	260 265 270	
55	GGC CCG GGG GTC CCG GGG GAG GTG GAG ATG GTG AAG GGG CAG CCG TTC	864
	Gly Pro Gly Val Pro Gly Glu Val Glu Met Val Lys Gly Gln Pro Phe	
	275 280 285	
	GAG GTC GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC	
	Tyr Gly Met Val Ser Ser Ala Tyr Asp His Val Arg Lys Thr Arg Val	
	305 310 315 320	
55	GAG GTC GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC	960
	Tyr Gly Met Val Ser Ser Ala Tyr Asp His Val Arg Lys Thr Arg Val	
	305 310 315 320	

	GCC ATC AAG AAG ATC AGC CCC TTC GAA CAT CAG ACC TAC TGC CAG CGC	1008
	Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr Tyr Cys Gln Arg	
	325 330 335	
5	ACG CTC CGG GAG ATC CAG ATC CTG CTG CGC TTC CGC CAT GAG AAT GTC	1056
	Thr Leu Arg Glu Ile Gln Ile Leu Leu Arg Phe Arg His Glu Asn Val	
	340 345 350	
10	ATC GGC ATC CGA GAC ATT CTG CGG GCG TCC ACC CTG GAA GCC ATG AGA	1104
	Ile Gly Ile Arg Asp Ile Leu Arg Ala Ser Thr Leu Glu Ala Met Arg	
	355 360 365	
15	GAT GTC TAC ATT GTG CAG GAC CTG ATG GAG ACT GAC CTG TAC AAG TTG	1152
	Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys Leu	
	370 375 380	
20	CTG AAA AGC CAG CAG CTG AGC AAT GAC CAT ATC TGC TAC TTC CTC TAC	1200
	Leu Lys Ser Gln Gln Leu Ser Asn Asp His Ile Cys Tyr Phe Leu Tyr	
	385 390 395 400	
25	CAG ATC CTG CGG GGC CTC AAG TAC ATC CAC TCC GCC AAC GTG CTC CAC	1248
	Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala Asn Val Leu His	
	405 410 415	
30	CGA GAT CTA AAG CCC TCC AAC CTG CTC AGC AAC ACC ACC TGC GAC CTT	1296
	Arg Asp Leu Lys Pro Ser Asn Leu Leu Ser Asn Thr Thr Cys Asp Leu	
	420 425 430	
35	AAG ATT TGT GAT TTC GGC CTG GCC CGG ATT GCC GAT CCT GAG CAT GAC	1344
	Lys Ile Cys Asp Phe Gly Leu Ala Arg Ile Ala Asp Pro Glu His Asp	
	435 440 445	
40	CAC ACC GGC TTC CTG ACG GAG TAT GTG GCT ACG CGC TGG TAC CGG GCC	1392
	His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg Trp Tyr Arg Ala	
	450 455 460	
45	CCA GAG ATC ATG CTG AAC TCC AAG GGC TAT ACC AAG TCC ATC GAC ATC	1440
	Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys Ser Ile Asp Ile	
	465 470 475 480	
50	TGG TCT GTG GGC TGC ATT CTG GCT GAG ATG CTC TCT AAC CGG CCC ATC	1488
	Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser Asn Arg Pro Ile	
	485 490 495	
55	TTC CCT GGC AAG CAC TAC CTG GAT CAG CTC AAC CAC ATT CTG GGC ATC	1536
	Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His Ile Leu Gly Ile	
	500 505	
60	CTG GAG TAC CTA CAG TCT CTG CCC TCC AAG ACC AAG GTG GCT TGG	1632
	Ala Arg Asn Tyr Leu Gln Ser Leu Pro Ser Lys Thr Lys Val Ala Thr	
	530 535	

69

	GCC	AAG	CTT	TTC	CCC	AAG	TCA	GAC	TCC	AAA	GCC	CTT	GAC	CTG	CTG	GAC	1680
	Ala	Lys	Leu	Phe	Pro	Lys	Ser	Asp	Ser	Lys	Ala	Leu	Asp	Leu	Leu	Asp	
	545					550					555					560	
5	CGG	ATG	TTA	ACC	TTT	AAC	CCC	AAT	AAA	CGG	ATC	ACA	GTG	GAG	GAA	GCG	1728
	Arg	Met	Leu	Thr	Phe	Asn	Pro	Asn	Lys	Arg	Ile	Thr	Val	Glu	Glu	Ala	
					565					570						575	
	CTG	GCT	CAC	CCC	TAC	CTG	GAG	CAG	TAC	TAT	GAC	CCG	ACG	GAT	GAG	CCA	1776
10	Leu	Ala	His	Pro	Tyr	Leu	Glu	Gln	Tyr	Tyr	Asp	Pro	Thr	Asp	Glu	Pro	
				580					585					590			
	GTG	GCC	GAG	GAG	CCC	TTC	ACC	TTC	GCC	ATG	GAG	CTG	GAT	GAC	CTA	CCT	1824
15	Val	Ala	Glu	Glu	Pro	Phe	Thr	Phe	Ala	Met	Glu	Leu	Asp	Asp	Leu	Pro	
			595					600					605				
	AAG	GAG	CGG	CTG	AAG	GAG	CTC	ATC	TTC	CAG	GAG	ACA	GCA	CGC	TTC	CAG	1872
	Lys	Glu	Arg	Leu	Lys	Glu	Leu	Ile	Phe	Gln	Glu	Thr	Ala	Arg	Phe	Gln	
		610					615					620					
20	CCC	GGA	GTG	CTG	GAG	GCC	C	CCTAG									1896
	Pro	Gly	Val	Leu	Glu	Ala	Pro										
	625					630											
25	(2) INFORMATION FOR SEQ ID NO:39:																
	(i) SEQUENCE CHARACTERISTICS:																
	(A) LENGTH: 631 amino acids																
30	(B) TYPE: amino acid																
	(C) STRANDEDNESS: single																
	(D) TOPOLOGY: linear																
	(ii) MOLECULE TYPE: protein																
35	(v) FRAGMENT TYPE: internal																
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:																
40	Met	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	
	1				5					10					15		
	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	
				20					25					30			
	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	
			35					40					45				
45	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val			

	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn
	145					150					155					160
	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser
					165					170					175	
5	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly
				180					185					190		
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu
			195					200					205			
10	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe
	210						215					220				
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser
	225					230					235				240	
	Gly	Leu	Arg	Ser	Arg	Ala	Gln	Ala	Ser	Asn	Ser	Thr	Met	Ala	Ala	Ala
					245					250					255	
15	Ala	Ala	Gln	Gly	Gly	Gly	Gly	Glu	Pro	Arg	Arg	Thr	Glu	Gly	Val	
				260				265					270			
	Gly	Pro	Gly	Val	Pro	Gly	Glu	Val	Glu	Met	Val	Lys	Gly	Gln	Pro	Phe
				275				280					285			
20	Asp	Val	Gly	Pro	Arg	Tyr	Thr	Gln	Leu	Gln	Tyr	Ile	Gly	Glu	Gly	Ala
	290						295					300				
	Tyr	Gly	Met	Val	Ser	Ser	Ala	Tyr	Asp	His	Val	Arg	Lys	Thr	Arg	Val
	305					310					315				320	
	Ala	Ile	Lys	Lys	Ile	Ser	Pro	Phe	Glu	His	Gln	Thr	Tyr	Cys	Gln	Arg
					325					330					335	
25	Thr	Leu	Arg	Glu	Ile	Gln	Ile	Leu	Leu	Arg	Phe	Arg	His	Glu	Asn	Val
				340				345						350		
	Ile	Gly	Ile	Arg	Asp	Ile	Leu	Arg	Ala	Ser	Thr	Leu	Glu	Ala	Met	Arg
			355					360					365			
30	Asp	Val	Tyr	Ile	Val	Gln	Asp	Leu	Met	Glu	Thr	Asp	Leu	Tyr	Lys	Leu
	370						375					380				
	Leu	Lys	Ser	Gln	Gln	Leu	Ser	Asn	Asp	His	Ile	Cys	Tyr	Phe	Leu	Tyr
	385					390					395				400	
	Gln	Ile	Leu	Arg	Gly	Leu	Lys	Tyr	Ile	His	Ser	Ala	Asn	Val	Leu	His
					405					410					415	
35	Arg	Asp	Leu	Lys	Pro	Ser	Asn	Leu	Leu	Ser	Asn	Thr	Thr	Cys	Asp	Leu
				420					425					430		
	Lys	Ile	Cys	Asp	Phe	Gly	Leu	Ala	Arg	Ile	Ala	Asp	Pro	Glu	His	Asp
			435					440					445			
40	His	Thr	Gly	Phe	Leu	Thr	Glu	Tyr	Val	Ala	Thr	Arg	Trp	Tyr	Arg	Ala
	450						455					460				
	Pro	Glu	Ile	Met	Leu	Asn	Ser	Lys	Gly	Tyr	Thr	Lys	Ser	Ile	Asp	Ile
	465					470										

71

Val Ala Glu Glu Pro Phe Thr Phe Ala Met Glu Leu Asp Asp Leu Pro
 595 600 605
 Lys Glu Arg Leu Lys Glu Leu Ile Phe Gln Glu Thr Ala Arg Phe Gln
 610 615 620
 5 Pro Gly Val Leu Glu Ala Pro
 625 630

(2) INFORMATION FOR SEQ ID NO:40:

10 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1818 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

20

- (A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...1815
 (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

25 ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG 48
 Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1 5 10 15

30 GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC 96
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
 20 25 30

35 GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC 144
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
 35 40 45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC 192
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 50 55 60

40 CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG 240
 Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
 65 70 75 80

45 CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG 288
 Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
 85 90 95

CGC ACC ATG TTC TTT

55 GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG 364
 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
 115 120 125

72

	ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC	432
	Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr	
	130 135 140	
5	AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC	480
	Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn	
	145 150 155 160	
10	GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC	528
	Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser	
	165 170 175	
15	GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC	576
	Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly	
	180 185 190	
20	CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG	624
	Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu	
	195 200 205	
25	AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC	672
	Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe	
	210 215 220	
30	GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC	720
	Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser	
	225 230 235 240	
35	GGA CTC AGA TCT CGA GTA ACC ATG GCG GCG GCG GCG GCG GCG GGC CCG	768
	Gly Leu Arg Ser Arg Val Thr Met Ala Ala Ala Ala Ala Gly Pro	
	245 250 255	
40	GAG ATG GTC CGC GGG CAG GTG TTC GAC GTG GGG CCG CGC TAC ACT AAT	816
	Glu Met Val Arg Gly Gln Val Phe Asp Val Gly Pro Arg Tyr Thr Asn	
	260 265 270	
45	CTC TCG TAC ATC GGA GAA GGC GCC TAC GGC ATG GTT TGT TCT GCT TAT	864
	Leu Ser Tyr Ile Gly Glu Gly Ala Tyr Gly Met Val Cys Ser Ala Tyr	
	275 280 285	
50	GAT AAT CTC AAC AAA GTT CGA GTT GCT ATC AAG AAA ATC AGT CCT TTT	912
	Asp Asn Leu Asn Lys Val Arg Val Ala Ile Lys Lys Ile Ser Pro Phe	
	290 295 300	
55	GAG CAC CAG ACC TAC TGT CAG AGA ACC CTG AGA GAG ATA AAA ATC CTA	960
	Glu His Gln Thr Tyr Cys Gln Arg Thr Leu Arg Glu Ile Lys Ile Leu	
	305 310 315 320	
	CTG GGC TTC TAT GAG GAG ATG AAA GAT GTA TAT ATA GTA CAG GAC CTC	1056
	Ala Pro Thr Ile Glu Gln Met Lys Asp Val Tyr Ile Val Gln Asp Leu	
	340 345 350	

73

	ATG GAG ACA GAT CTT TAC AAG CTC TTG AAG ACA CAG CAC CTC AGC AAT	1104
	Met Glu Thr Asp Leu Tyr Lys Leu Leu Lys Thr Gln His Leu Ser Asn	
	355 360 365	
5	GAT CAT ATC TGC TAT TTT CTT TAT CAG ATC CTG AGA GGA TTA AAG TAT	1152
	Asp His Ile Cys Tyr Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr	
	370 375 380	
10	ATA CAT TCA GCT AAT GTT CTG CAC CGT GAC CTC AAG CCT TCC AAC CTC	1200
	Ile His Ser Ala Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu	
	385 390 395 400	
15	CTG CTG AAC ACC ACT TGT GAT CTC AAG ATC TGT GAC TTT GGC CTT GCC	1248
	Leu Leu Asn Thr Thr Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala	
	405 410 415	
20	CGT GTT GCA GAT CCA GAC CAT GAT CAT ACA GGG TTC TTG ACA GAG TAT	1296
	Arg Val Ala Asp Pro Asp His Asp His Thr Gly Phe Leu Thr Glu Tyr	
	420 425 430	
25	GTA GCC ACG CGT TGG TAC AGA GCT CCA GAA ATT ATG TTG AAT TCC AAG	1344
	Val Ala Thr Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys	
	435 440 445	
30	GGT TAT ACC AAG TCC ATT GAT ATT TGG TCT GTG GGC TGC ATC CTG GCA	1392
	Gly Tyr Thr Lys Ser Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala	
	450 455 460	
35	GAG ATG CTA TCC AAC AGG CCT ATC TTC CCA GGA AAG CAT TAC CTT GAC	1440
	Glu Met Leu Ser Asn Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp	
	465 470 475 480	
40	CAG CTG AAT CAC ATC CTG GGT ATT CTT GGA TCT CCA TCA CAG GAA GAT	1488
	Gln Leu Asn His Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp	
	485 490 495	
45	CTG AAT TGT ATA ATA AAT TTA AAA GCT AGA AAC TAT TTG CTT TCT CTC	1536
	Leu Asn Cys Ile Ile Asn Leu Lys Ala Arg Asn Tyr Leu Leu Ser Leu	
	500 505 510	
50	CCG CAC AAA AAT AAG GTG CCG TGG AAC AGG TTG TTC CCA AAC GCT GAC	1584
	Pro His Lys Asn Lys Val Pro Trp Asn Arg Leu Phe Pro Asn Ala Asp	
	515 520 525	
55	TCC AAA GCT CTG GAT TTA CTG GAT AAA ATG TTG ACA TTT AAC CCT CAC	1632
	Ser Lys Ala Leu Asp Leu Leu Asp Lys Met Leu Thr Phe Asn Pro His	
	530 535 540	
	AAG AGG ATT GAT TAT TTT CTT TAT CAG ATC CTG AGA GGA TTA AAG TAT	1728
	Tyr Tyr Asp Pro Ser Asp Glu Pro Ile Ala Glu Ala Pro Phe Lys Phe	
	565 570 575	

74

GAC ATG GAG CTG GAC GAC TTA CCT AAG GAG AAG CTC AAA GAA CTC ATT 1776
Asp Met Glu Leu Asp Asp Leu Pro Lys Glu Lys Leu Lys Glu Leu Ile
580 585 590

5 TTT GAA GAG ACT GCT CGA TTC CAG CCA GGA TAC AGA TCT TAA 1818
 Phe Glu Glu Thr Ala Arg Phe Gln Pro Gly Tyr Arg Ser
 595 600 605

10 (2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 605 amino acids

(B) TYPE: amino acid

15 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

[illegible][illegible]

75

Leu Ser Tyr Ile Gly Glu Gly Ala Tyr Gly Met Val Cys Ser Ala Tyr
 275 280 285
 Asp Asn Leu Asn Lys Val Arg Val Ala Ile Lys Lys Ile Ser Pro Phe
 290 295 300
 5 Glu His Gln Thr Tyr Cys Gln Arg Thr Leu Arg Glu Ile Lys Ile Leu
 305 310 315 320
 Leu Arg Phe Arg His Glu Asn Ile Ile Gly Ile Asn Asp Ile Ile Arg
 325 330 335
 10 Ala Pro Thr Ile Glu Gln Met Lys Asp Val Tyr Ile Val Gln Asp Leu
 340 345 350
 Met Glu Thr Asp Leu Tyr Lys Leu Leu Lys Thr Gln His Leu Ser Asn
 355 360 365
 Asp His Ile Cys Tyr Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr
 370 375 380
 15 Ile His Ser Ala Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu
 385 390 395 400
 Leu Leu Asn Thr Thr Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala
 405 410 415
 20 Arg Val Ala Asp Pro Asp His Asp His Thr Gly Phe Leu Thr Glu Tyr
 420 425 430
 Val Ala Thr Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys
 435 440 445
 Gly Tyr Thr Lys Ser Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala
 450 455 460
 25 Glu Met Leu Ser Asn Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp
 465 470 475 480
 Gln Leu Asn His Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp
 485 490 495
 30 Leu Asn Cys Ile Ile Asn Leu Lys Ala Arg Asn Tyr Leu Leu Ser Leu
 500 505 510
 Pro His Lys Asn Lys Val Pro Trp Asn Arg Leu Phe Pro Asn Ala Asp
 515 520 525
 Ser Lys Ala Leu Asp Leu Leu Asp Lys Met Leu Thr Phe Asn Pro His
 530 535 540
 35 Lys Arg Ile Glu Val Glu Gln Ala Leu Ala His Pro Tyr Leu Glu Gln
 545 550 555 560
 Tyr Tyr Asp Pro Ser Asp Glu Pro Ile Ala Glu Ala Pro Phe Lys Phe
 565 570 575
 40 Asp Met Glu Leu Asp Asp Leu Pro Lys Glu Lys Leu Lys Glu Leu Ile
 580 585 590
 Phe Glu Glu Thr Ala Arg Phe Gln Pro Gly Tyr Arg Ser
 595 600 605

(2) INFORMATION FOR SEQ ID NO:42:

45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2529 base pairs

(B) TYPE: nucleic acid

EX- FEATURE:

55

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 1-2529

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

5	ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG	48
	Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu	
	1 5 10 15	
10	GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC	96
	Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly	
	20 25 30	
15	GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTC ACC CTG AAG TTC ATC	144
	Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile	
	35 40 45	
20	TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC	192
	Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr	
	50 55 60	
25	CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG	240
	Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys	
	65 70 75 80	
30	CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG	288
	Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu	
	85 90 95	
35	CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG	336
	Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu	
	100 105 110	
40	GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC	384
	Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly	
	115 120 125	
45	ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC	432
	Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr	
	130 135 140	
50	AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC	480
	Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn	
	145 150 155 160	
55	GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC	528
	Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser	
	165 170 175	
60	GTG CAG CTG TAC GGC GAC GAC GGC AAC TAC CTG AGC ACC CAG TCC GCC CTG	576
	Val Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu	
	180 185 190 195 200 205	
65	CTG GAG GGC GAC GGC GAT GCC ACC TAC GGC AAG CTC ACC CTG AAG TTC ATC	624
	Leu Glu Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile	
	210 215 220 225 230 235	

77

	AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe 210 215 220	672
5	GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser 225 230 235 240	720
10	GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCG TCA ATG GAG CTG GAA Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ser Met Glu Leu Glu 245 250 255	768
15	AAC ATC GTG GCC AAC ACG GTC TTG CTG AAA GCC AGG GAA GGG GGC GGA Asn Ile Val Ala Asn Thr Val Leu Leu Lys Ala Arg Glu Gly Gly Gly 260 265 270	816
20	GGA AAG CGC AAA GGG AAA AGC AAG AAG TGG AAA GAA ATC CTG AAG TTC Gly Lys Arg Lys Gly Lys Ser Lys Lys Trp Lys Glu Ile Leu Lys Phe 275 280 285	864
25	CCT CAC ATT AGC CAG TGT GAA GAC CTC CGA AGG ACC ATA GAC AGA GAT Pro His Ile Ser Gln Cys Glu Asp Leu Arg Arg Thr Ile Asp Arg Asp 290 295 300	912
30	TAC TGC AGT TTA TGT GAC AAG CAG CCA ATC GGG AGG CTG CTT TTC CGG Tyr Cys Ser Leu Cys Asp Lys Gln Pro Ile Gly Arg Leu Leu Phe Arg 305 310 315 320	960
35	CAG TTT TGT GAA ACC AGG CCT GGG CTG GAG TGT TAC ATT CAG TTC CTG Gln Phe Cys Glu Thr Arg Pro Gly Leu Glu Cys Tyr Ile Gln Phe Leu 325 330 335	1008
40	GAC TCC GTG GCA GAA TAT GAA GTT ACT CCA GAT GAA AAA CTG GGA GAG Asp Ser Val Ala Glu Tyr Glu Val Thr Pro Asp Glu Lys Leu Gly Glu 340 345 350	1056
45	AAA GGG AAG GAA ATT ATG ACC AAG TAC CTC ACC CCA AAG TCC CCT GTT Lys Gly Lys Glu Ile Met Thr Lys Tyr Leu Thr Pro Lys Ser Pro Val 355 360 365	1104
50	TTC ATA GCC CAA GTT GGC CAA GAC CTG GTC TCC CAG ACG GAG GAG AAG Phe Ile Ala Gln Val Gly Gln Asp Leu Val Ser Gln Thr Glu Glu Lys 370 375 380	1152
55	CTC CTA CAG AAG CCG TGC AAA GAA CTC TTT TCT GCC TGT GCA CAG TCT Leu Leu Gln Lys Pro Cys Lys Glu Leu Phe Ser Ala Cys Ala Gln Ser 385 390 395 400	1200
60	GTC CAC GAG TAC CTC AAG TGG TGG TTT GAA AGG CAA CCG Ret Phe Phe Asp Arg Phe Leu Gln Trp Lys Trp Leu Glu Arg Gln Pro 420 425 430	1296

78

	GTG ACC AAA AAC ACT TTC AGG CAG TAT CGA GTG CTA GGA AAA GGG GGC Val Thr Lys Asn Thr Phe Arg Gln Tyr Arg Val Leu Gly Lys Gly Gly 435 440 445	1344
5	TTC GGG GAG GTC TGT GCC TGC CAG GTT CGG GCC ACG GGT AAA ATG TAT Phe Gly Glu Val Cys Ala Cys Gln Val Arg Ala Thr Gly Lys Met Tyr 450 455 460	1392
10	GCC TGC AAG CGC TTG GAG AAG AAG AGG ATC AAA AAG AGG AAA GGG GAG Ala Cys Lys Arg Leu Glu Lys Lys Arg Ile Lys Lys Arg Lys Gly Glu 465 470 475 480	1440
15	TCC ATG GCC CTC AAT GAG AAG CAG ATC CTC CAG AAG GTC AAC AGT CAG Ser Met Ala Leu Asn Glu Lys Gln Ile Leu Glu Lys Val Asn Ser Gln 485 490 495	1488
20	TTT GTG GTC AAC CTG GCC TAT GCC TAC GAG ACC AAG GAT GCA CTG TGC Phe Val Val Asn Leu Ala Tyr Ala Tyr Glu Thr Lys Asp Ala Leu Cys 500 505 510	1536
25	TTG GTC CTG ACC ATC ATG AAT GGG GGT GAC CTG AAG TTC CAC ATC TAC Leu Val Leu Thr Ile Met Asn Gly Gly Asp Leu Lys Phe His Ile Tyr 515 520 525	1584
30	AAC ATG GGC AAC CCT GGC TTC GAG GAG GAG CGG GCC TTG TTT TAT GCG Asn Met Gly Asn Pro Gly Phe Glu Glu Glu Arg Ala Leu Phe Tyr Ala 530 535 540	1632
35	GCA GAG ATC CTC TGC GGC TTA GAA GAC CTC CAC CGT GAG AAC ACC GTC Ala Glu Ile Leu Cys Gly Leu Glu Asp Leu His Arg Glu Asn Thr Val 545 550 555 560	1680
40	TAC CGA GAT CTG AAA CCT GAA AAC ATC CTG TTA GAT GAT TAT GGC CAC Tyr Arg Asp Leu Lys Pro Glu Asn Ile Leu Leu Asp Asp Tyr Gly His 565 570 575	1728
45	ATT AGG ATC TCA GAC CTG GGC TTG GCT GTG AAG ATC CCC GAG GGA GAC Ile Arg Ile Ser Asp Leu Gly Leu Ala Val Lys Ile Pro Glu Gly Asp 580 585 590	1776
50	CTG ATC CGC GGC CGG GTG GGC ACT GTT GGC TAC ATG GCC CCC GAA GTC Leu Ile Arg Gly Arg Val Gly Thr Val Gly Tyr Met Ala Pro Glu Val 595 600 605	1824
55	CTG AAC AAC CAG AGG TAC GGC CTG AGC CCC GAC TAC TGG GGC CTT GGC Leu Asn Asn Gln Arg Tyr Gly Leu Ser Pro Asp Tyr Trp Gly Leu Gly 610 615 620	1872
60	CTG AAC AAC CAG AGG TAC GGC CTG AGC CCC GAC TAC TGG GGC CTT GGC Leu Asn Asn Gln Arg Tyr Gly Leu Ser Pro Asp Tyr Trp Gly Leu Gly 620 625 630	1920
65	CTG AAC AAC CAG AGG TAC GGC CTG AGC CCC GAC TAC TGG GGC CTT GGC Leu Asn Asn Gln Arg Tyr Gly Leu Ser Pro Asp Tyr Trp Gly Leu Gly 630 635 640	1968

79

	GAG GAG GTG TAC TCC CAC AAG TTC TCC GAG GAG GCC AAG TCC ATC TGC	2016
	Glu Glu Val Tyr Ser His Lys Phe Ser Glu Glu Ala Lys Ser Ile Cys	
	660 665 670	
5	AAG ATG CTG CTC ACG AAA GAT GCG AAG CAG AGG CTG GGC TGC CAG GAG	2064
	Lys Met Leu Leu Thr Lys Asp Ala Lys Gln Arg Leu Gly Cys Gln Glu	
	675 680 685	
10	GAG GGG GCT GCA GAG GTC AAG AGA CAC CCC TTC TTC AGG AAC ATG AAC	2112
	Glu Gly Ala Ala Glu Val Lys Arg His Pro Phe Phe Arg Asn Met Asn	
	690 695 700	
15	TTC AAG CGC TTA GAA GCC GGG ATG TTG GAC CCT CCC TTC GTT CCA GAC	2160
	Phe Lys Arg Leu Glu Ala Gly Met Leu Asp Pro Pro Phe Val Pro Asp	
	705 710 715 720	
20	CCC CGC GCT GTG TAC TGT AAG GAC GTG CTG GAC ATC GAG CAG TTC TCC	2208
	Pro Arg Ala Val Tyr Cys Lys Asp Val Leu Asp Ile Glu Gln Phe Ser	
	725 730 735	
25	ACT GTG AAG GGC GTC AAT CTG GAC CAC ACA GAC GAC GAC TTC TAC TCC	2256
	Thr Val Lys Gly Val Asn Leu Asp His Thr Asp Asp Asp Phe Tyr Ser	
	740 745 750	
30	AAG TTC TCC ACG GGC TCT GTG TCC ATC CCA TGG CAA AAC GAG ATG ATA	2304
	Lys Phe Ser Thr Gly Ser Val Ser Ile Pro Trp Gln Asn Glu Met Ile	
	755 760 765	
35	GAA ACA GAA TGC TTT AAG GAG CTG AAC GTG TTT GGA CCT AAT GGT ACC	2352
	Glu Thr Glu Cys Phe Lys Glu Leu Asn Val Phe Gly Pro Asn Gly Thr	
	770 775 780	
40	CTC CCG CCA GAT CTG AAC AGA AAC CAC CCT CCG GAA CCG CCC AAG AAA	2400
	Leu Pro Pro Asp Leu Asn Arg Asn His Pro Pro Glu Pro Pro Lys Lys	
	785 790 795 800	
45	GGG CTG CTC CAG AGA CTC TTC AAG CGG CAG CAT CAG AAC AAT TCC AAG	2448
	Gly Leu Leu Gln Arg Leu Phe Lys Arg Gln His Gln Asn Asn Ser Lys	
	805 810 815	
50	AGT TCG CCC AGC TCC AAG ACC AGT TTT AAC CAC CAC ATA AAC TCA AAC	2496
	Ser Ser Pro Ser Ser Lys Thr Ser Phe Asn His His Ile Asn Ser Asn	
	820 825 830	
55	CAT GTC AGC TCG AAC TCC ACC GGA AGC AGC TAG	2529
	His Val Ser Ser Asn Ser Thr Gly Ser Ser	
	835 840	

SEQUENCE: AAGATTTTCTTCT
 LENGTH: 842 amino acids

(B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

```

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1           5           10           15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
10           20           25           30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
           35           40           45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
50           55           60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
15           65           70           75           80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
           85           90           95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
20           100          105          110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
           115          120          125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
           130          135          140
25 Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
           145          150          155          160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
           165          170          175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
30           180          185          190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
           195          200          205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
           210          215          220
35 Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
           225          230          235          240
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ser Met Glu Leu Glu
           245          250          255
Asn Ile Val Ala Asn Thr Val Leu Leu Lys Ala Arg Glu Gly Gly Gly
40           260          265          270
Gly Lys Arg Lys Gly Lys Ser Lys Lys Trp Lys Glu Ile Leu Lys Phe
           275          280          285
Pro His Ile Ser Gln Cys Glu Asp Leu Arg Arg Thr Ile Asp Arg Asp
           290          295          300
45 Tyr Cys Ser Leu Cys Asp Lys Gln Pro Ile Gly Arg Leu Leu Phe Arg
           305          310          315          320
Gln Phe Cys Glu Thr Arg Pro Gly Leu Glu Cys Tyr Ile Gln Phe Leu
           325          330
Asp Ser Val ...
           335
           340
           345
           350
           355
           360
           365
           370          375          380
55 Leu Leu Gln Lys Pro Cys Lys Glu Leu Phe Ser Ala Cys Ala Gln Ser
           385          390

```

	Val	His	Glu	Tyr	Leu	Arg	Gly	Glu	Pro	Phe	His	Glu	Tyr	Leu	Asp	Ser
					405					410					415	
	Met	Phe	Phe	Asp	Arg	Phe	Leu	Gln	Trp	Lys	Trp	Leu	Glu	Arg	Gln	Pro
				420					425					430		
5	Val	Thr	Lys	Asn	Thr	Phe	Arg	Gln	Tyr	Arg	Val	Leu	Gly	Lys	Gly	Gly
			435					440					445			
	Phe	Gly	Glu	Val	Cys	Ala	Cys	Gln	Val	Arg	Ala	Thr	Gly	Lys	Met	Tyr
		450					455					460				
10	Ala	Cys	Lys	Arg	Leu	Glu	Lys	Lys	Arg	Ile	Lys	Lys	Arg	Lys	Gly	Glu
	465					470					475					480
	Ser	Met	Ala	Leu	Asn	Glu	Lys	Gln	Ile	Leu	Glu	Lys	Val	Asn	Ser	Gln
				485						490				495		
	Phe	Val	Val	Asn	Leu	Ala	Tyr	Ala	Tyr	Glu	Thr	Lys	Asp	Ala	Leu	Cys
				500					505					510		
15	Leu	Val	Leu	Thr	Ile	Met	Asn	Gly	Gly	Asp	Leu	Lys	Phe	His	Ile	Tyr
			515					520					525			
	Asn	Met	Gly	Asn	Pro	Gly	Phe	Glu	Glu	Glu	Arg	Ala	Leu	Phe	Tyr	Ala
		530					535					540				
20	Ala	Glu	Ile	Leu	Cys	Gly	Leu	Glu	Asp	Leu	His	Arg	Glu	Asn	Thr	Val
	545					550					555					560
	Tyr	Arg	Asp	Leu	Lys	Pro	Glu	Asn	Ile	Leu	Leu	Asp	Asp	Tyr	Gly	His
				565						570					575	
	Ile	Arg	Ile	Ser	Asp	Leu	Gly	Leu	Ala	Val	Lys	Ile	Pro	Glu	Gly	Asp
				580					585					590		
25	Leu	Ile	Arg	Gly	Arg	Val	Gly	Thr	Val	Gly	Tyr	Met	Ala	Pro	Glu	Val
			595					600					605			
	Leu	Asn	Asn	Gln	Arg	Tyr	Gly	Leu	Ser	Pro	Asp	Tyr	Trp	Gly	Leu	Gly
		610					615					620				
30	Cys	Leu	Ile	Tyr	Glu	Met	Ile	Glu	Gly	Gln	Ser	Pro	Phe	Arg	Gly	Arg
	625					630					635					640
	Lys	Glu	Lys	Val	Lys	Arg	Glu	Glu	Val	Asp	Arg	Arg	Val	Leu	Glu	Thr
				645						650					655	
	Glu	Glu	Val	Tyr	Ser	His	Lys	Phe	Ser	Glu	Glu	Ala	Lys	Ser	Ile	Cys
				660					665					670		
35	Lys	Met	Leu	Leu	Thr	Lys	Asp	Ala	Lys	Gln	Arg	Leu	Gly	Cys	Gln	Glu
			675					680					685			
	Glu	Gly	Ala	Ala	Glu	Val	Lys	Arg	His	Pro	Phe	Phe	Arg	Asn	Met	Asn
		690					695					700				
40	Phe	Lys	Arg	Leu	Glu	Ala	Gly	Met	Leu	Asp	Pro	Pro	Phe	Val	Pro	Asp
	705					710					715					720
	Pro	Arg	Ala	Val	Tyr	Cys	Lys	Asp	Val	Leu	Asp	Ile	Glu	Gln	Phe	Ser
			</													

5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1902 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1899
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

20 ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu 48
1 5 10 15
GTC GAG CTG GAG

25 GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly 96

30 GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile 144
 35 40 45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 50 55 60

35 CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys 240
65 70 75 80

40 CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu 288
85 90 95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG
 45 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu 336
 100 105 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ser

135 140

55 AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAC AAC
Asn Tyr Asn Ser His Asn Val Thr Thr Met Leu Ile Thr Thr

83

	145		150		155		160	
5	GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC							528
	Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser							
		165			170		175	
10	GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC							576
	Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly							
		180			185		190	
15	CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG							624
	Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu							
		195			200		205	
20	AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC							672
	Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe							
		210			215		220	
25	GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC							720
	Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser							
		225			230		235	240
30	GGA CTC AGA TCT CGA GCT CGA GCC ATC ATG AGC AGA AGC AAG CGT GAC							768
	Gly Leu Arg Ser Arg Ala Arg Ala Ile Met Ser Arg Ser Lys Arg Asp							
		245			250		255	
35	AAC AAT TTT TAT AGT GTA GAG ATT GGA GAT TCT ACA TTC ACA GTC CTG							816
	Asn Asn Phe Tyr Ser Val Glu Ile Gly Asp Ser Thr Phe Thr Val Leu							
		260			265		270	
40	AAA CGA TAT CAG AAT TTA AAA CCT ATA GGC TCA GGA GCT CAA GGA ATA							864
	Lys Arg Tyr Gln Asn Leu Lys Pro Ile Gly Ser Gly Ala Gln Gly Ile							
		275			280		285	
45	GTA TGC GCA GCT TAT GAT GCC ATT CTT GAA AGA AAT GTT GCA ATC AAG							912
	Val Cys Ala Ala Tyr Asp Ala Ile Leu Glu Arg Asn Val Ala Ile Lys							
		290			295		300	
50	AAG CTA AGC CGA CCA TTT CAG AAT CAG ACT CAT GCC AAG CGG GCC TAC							960
	Lys Leu Ser Arg Pro Phe Gln Asn Gln Thr His Ala Lys Arg Ala Tyr							
		305			310		315	320
55	AGA GAG CTA GTT CTT ATG AAA TGT GTT AAT CAC AAA AAT ATA ATT GGC							1008
	Arg Glu Leu Val Leu Met Lys Cys Val Asn His Lys Asn Ile Ile Gly							
		325			330		335	
60	CTT TTG AAT GTT TTC ACA CCA CAG AAA TCC CTA GAA GAA TTT CAA GAT							1056
	Leu Leu Asn Val Phe Thr Pro Gln Lys Ser Thr Thr Thr Thr Thr Thr							
		340			345		350	
65	CAG ATG GAG CTA GAT CAT GAA AGA ATG TCC TAC CTT CTC TAT CAG ATC							1104
	Gln Met Glu Leu Asn His Gln Asn Met Thr Thr Thr Thr Thr Thr							
		355			360		365	

380

SUBSTITUTE SHEET (RULE 26)

85

595 600 605

GTT ATG GAC TTG GAG GAG AGA ACC AAG AAT GGA GTT ATA CGG GGG CAG 1872
 Val Met Asp Leu Glu Glu Arg Thr Lys Asn Gly Val Ile Arg Gly Gln
 5 610 615 620

CCC TCT CCT TTA GCA CAG GTG CAG CAG TGA 1902
 Pro Ser Pro Leu Ala Gln Val Gln Gln
 10 625 630

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:

- 15 (A) LENGTH: 633 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

- 20 (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

25 Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1 5 10 15
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
 20 25 30
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
 30 35 40 45
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 50 55 60
 Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
 65 70 75 80
 35 Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
 85 90 95
 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
 100 105 110
 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
 40 115 120 125
 Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
 130 135 140
 Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
 145 150 155 160
 45 Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
 165 170 175
 Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
 180 185
 Pro Val ...
 ...
 ...
 ...
 225 230 235 240
 55 Gly Leu Arg Ser Arg Ala Arg Ala Ile Met Ser Arg Ser Lys Arg Ser
 245

86

	Asn	Asn	Phe	Tyr	Ser	Val	Glu	Ile	Gly	Asp	Ser	Thr	Phe	Thr	Val	Leu
			260						265					270		
	Lys	Arg	Tyr	Gln	Asn	Leu	Lys	Pro	Ile	Gly	Ser	Gly	Ala	Gln	Gly	Ile
			275					280					285			
5	Val	Cys	Ala	Ala	Tyr	Asp	Ala	Ile	Leu	Glu	Arg	Asn	Val	Ala	Ile	Lys
		290					295					300				
	Lys	Leu	Ser	Arg	Pro	Phe	Gln	Asn	Gln	Thr	His	Ala	Lys	Arg	Ala	Tyr
	305					310					315					320
	Arg	Glu	Leu	Val	Leu	Met	Lys	Cys	Val	Asn	His	Lys	Asn	Ile	Ile	Gly
10					325					330					335	
	Leu	Leu	Asn	Val	Phe	Thr	Pro	Gln	Lys	Ser	Leu	Glu	Glu	Phe	Gln	Asp
				340					345					350		
	Val	Tyr	Ile	Val	Met	Glu	Leu	Met	Asp	Ala	Asn	Leu	Cys	Gln	Val	Ile
		355						360					365			
15	Gln	Met	Glu	Leu	Asp	His	Glu	Arg	Met	Ser	Tyr	Leu	Leu	Tyr	Gln	Met
		370					375					380				
	Leu	Cys	Gly	Ile	Lys	His	Leu	His	Ser	Ala	Gly	Ile	Ile	His	Arg	Asp
	385					390					395					400
	Leu	Lys	Pro	Ser	Asn	Ile	Val	Val	Lys	Ser	Asp	Cys	Thr	Leu	Lys	Ile
20					405					410					415	
	Leu	Asp	Phe	Gly	Leu	Ala	Arg	Thr	Ala	Gly	Thr	Ser	Phe	Met	Met	Thr
				420					425					430		
	Pro	Tyr	Val	Val	Thr	Arg	Tyr	Tyr	Arg	Ala	Pro	Glu	Val	Ile	Leu	Gly
		435						440					445			
25	Met	Gly	Tyr	Lys	Glu	Asn	Val	Asp	Leu	Trp	Ser	Val	Gly	Cys	Ile	Met
		450				455						460				
	Gly	Glu	Met	Val	Cys	His	Lys	Ile	Leu	Phe	Pro	Gly	Arg	Asp	Tyr	Ile
	465					470					475					480
	Asp	Gln	Trp	Asn	Lys	Val	Ile	Glu	Gln	Leu	Gly	Thr	Pro	Cys	Pro	Glu
30					485					490					495	
	Phe	Met	Lys	Lys	Leu	Gln	Pro	Thr	Val	Arg	Thr	Tyr	Val	Glu	Asn	Arg
				500					505					510		
	Pro	Lys	Tyr	Ala	Gly	Tyr	Ser	Phe	Glu	Lys	Leu	Phe	Pro	Asp	Val	Leu
			515					520					525			
35	Phe	Pro	Ala	Asp	Ser	Glu	His	Asn	Lys	Leu	Lys	Ala	Ser	Gln	Ala	Arg
		530					535					540				
	Asp	Leu	Leu	Ser	Lys	Met	Leu	Val	Ile	Asp	Ala	Ser	Lys	Arg	Ile	Ser
	545					550					555					560
	Val	Asp	Glu	Ala	Leu	Gln	His	Pro	Tyr	Ile	Asn	Val	Trp	Tyr	Asp	Pro
40					565					570					575	
	Ser	Glu	Ala	Glu	Ala	Pro	Pro	Pro	Lys	Ile	Pro	Asp	Lys	Gln	Leu	Asp
				580					585					590		
	Glu	Arg	Glu	His	Thr	Ile	Glu	Glu	Trp	Lys	Glu	Leu	Ile	Tyr	Lys	Glu
		595						600					605			
45	Val	Met	Asp	Leu	Glu	Glu	Arg	Thr	Lys	Asn	Gly	Val	Ile	Arg	Gly	Gln
		610					615					620				
	Pro	Ser	Pro	Leu	Ala	Gln	Val	Gln	Gln							
	625					630										

55

(A) LENGTH: 1824 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

5

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...1821

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

10

ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG 48
 Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1 5 10 15

15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC 96
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
 20 25 30

20

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC 144
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
 35 40 45

25

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC 192
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 50 55 60

30

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG 240
 Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
 65 70 75 80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG 288
 Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
 85 90 95

35

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG 336
 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
 100 105 110

40

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC 384
 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
 115 120 125

45

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC 432
 Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
 130 135 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC 480
 Asn Tyr Asn Ser His Asn Val Thr Thr Thr Thr Thr Thr Thr Thr

165 170 175
 Gly His Asn Ile Glu Asp Gly Ser

55

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC CCC GAG CCC
 Val Gln Leu Ala Asp His Thr Thr Thr Thr Thr Thr Thr Thr

88

	180	185	190	
5	CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu 195 200 205	624		
10	AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe 210 215 220	672		
15	GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser 225 230 235 240	720		
20	GGA CTC AGA TCT CGA GGG AAA ATG TCT CAG GAG AGG CCC ACG TTC TAC Gly Leu Arg Ser Arg Gly Lys Met Ser Gln Glu Arg Pro Thr Phe Tyr 245 250 255	768		
25	CGG CAG GAG CTG AAC AAG ACA ATC TGG GAG GTG CCC GAG CGT TAC CAG Arg Gln Glu Leu Asn Lys Thr Ile Trp Glu Val Pro Glu Arg Tyr Gln 260 265 270	816		
30	AAC CTG TCT CCA GTG GGC TCT GGC GCC TAT GGC TCT GTG TGT GCT GCT Asn Leu Ser Pro Val Gly Ser Gly Ala Tyr Gly Ser Val Cys Ala Ala 275 280 285	864		
35	TTT GAC ACA AAA ACG GGG TTA CGT GTG GCA GTG AAG AAG CTC TCC AGA Phe Asp Thr Lys Thr Gly Leu Arg Val Ala Val Lys Lys Leu Ser Arg 290 295 300	912		
40	CCA TTT CAG TCC ATC ATT CAT GCG AAA AGA ACC TAC AGA GAA CTG CGG Pro Phe Gln Ser Ile Ile His Ala Lys Arg Thr Tyr Arg Glu Leu Arg 305 310 315 320	960		
45	TTA CTT AAA CAT ATG AAA CAT GAA AAT GTG ATT GGT CTG TTG GAC GTT Leu Leu Lys His Met Lys His Glu Asn Val Ile Gly Leu Leu Asp Val 325 330 335	1008		
50	TTT ACA CCT GCA AGG TCT CTG GAG GAA TTC AAT GAT GTG TAT CTG GTG Phe Thr Pro Ala Arg Ser Leu Glu Glu Phe Asn Asp Val Tyr Leu Val 340 345 350	1056		
55	ACC CAT CTC ATG GGG GCA GAT CTG AAC AAC ATT GTG AAA TGT CAG AAG Thr His Leu Met Gly Ala Asp Leu Asn Asn Ile Val Lys Cys Gln Lys 355 360 365	1104		
60	CTT ACA GAT GAC CAT GTT CAG TTC CTT ATC TAC CAA ATT CTC CGA GGT Leu Thr Asp Asp His Val Gln Phe Leu Thr Thr Thr Thr Thr Thr Thr 370 375 380 385 390 395 400	1152		
65	AGT AAT CTA GCT GTG AAT GAA GAC TGT GAG CTG AAG ATT CTG GAT TTC Ser Asn Leu Ala Val Asn Glu Asp Thr Thr Thr Thr Thr Thr Thr Thr 405 410 415 420 425 430 435 440 445 450	1200		

[illegible]

55 (ii) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 607 amino acids
(B) TYPE: amino acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

	Met	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu
10	1				5					10					15	
	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly
				20					25					30		
	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile
				35				40					45			
15	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr
	50						55					60				
	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys
	65					70					75				80	
	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu
20					85					90					95	
	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu
				100					105					110		
	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly
				115				120					125			
25	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr
	130						135					140				
	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn
	145					150					155				160	
	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser
30					165					170					175	
	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly
				180					185					190		
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu
				195				200					205			
35	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe
	210						215					220				
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser
	225					230					235				240	
	Gly	Leu	Arg	Ser	Arg	Gly	Lys	Met	Ser	Gln	Glu	Arg	Pro	Thr	Phe	Tyr
40					245					250					255	
	Arg	Gln	Glu	Leu	Asn	Lys	Thr	Ile	Trp	Glu	Val	Pro	Glu	Arg	Tyr	Gln
				260					265					270		
	Asn	Leu	Ser	Pro	Val	Gly	Ser	Gly	Ala	Tyr	Gly	Ser	Val	Cys	Ala	Ala
				275				280					285			
45	Phe	Asp	Thr	Lys	Thr	Gly	Leu	Arg	Val	Ala	Val	Lys	Lys	Leu	Ser	Arg
	290						295					300				
	Pro	Phe	Gln	Ser	Ile	Ile	His	Ala	Lys	Arg	Thr	Tyr	Arg	Glu	Leu	Arg
	305					310										
	Leu	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Thr

91

Leu Lys Tyr Ile His Ser Ala Asp Ile Ile His Arg Asp Leu Lys Pro
 385 390 395 400
 Ser Asn Leu Ala Val Asn Glu Asp Cys Glu Leu Lys Ile Leu Asp Phe
 405 410 415
 5 Gly Leu Ala Arg His Thr Asp Asp Glu Met Thr Gly Tyr Val Ala Thr
 420 425 430
 Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Trp Met His Tyr Asn
 435 440 445
 10 Gln Thr Val Asp Ile Trp Ser Val Gly Cys Ile Met Ala Glu Leu Leu
 450 455 460
 Thr Gly Arg Thr Leu Phe Pro Gly Thr Asp His Ile Asp Gln Leu Lys
 465 470 475 480
 Leu Ile Leu Arg Leu Val Gly Thr Pro Gly Ala Glu Leu Leu Lys Lys
 485 490 495
 15 Ile Ser Ser Glu Ser Ala Arg Asn Tyr Ile Gln Ser Leu Thr Gln Met
 500 505 510
 Pro Lys Met Asn Phe Ala Asn Val Phe Ile Gly Ala Asn Pro Leu Ala
 515 520 525
 20 Val Asp Leu Leu Glu Lys Met Leu Val Leu Asp Ser Asp Lys Arg Ile
 530 535 540
 Thr Ala Ala Gln Ala Leu Ala His Ala Tyr Phe Ala Gln Tyr His Asp
 545 550 555 560
 Pro Asp Asp Glu Pro Val Ala Asp Pro Tyr Asp Gln Ser Phe Glu Ser
 565 570 575
 25 Arg Asp Leu Leu Ile Asp Glu Trp Lys Ser Leu Thr Tyr Asp Glu Val
 580 585 590
 Ile Ser Phe Val Pro Pro Pro Leu Asp Gln Glu Glu Met Glu Ser
 595 600 605

30 (2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2907 base pairs

(B) TYPE: nucleic acid

35 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

40

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...2904

(D) OTHER INFORMATION:

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG
 Met Val Ser Lys Gly Glu Glu Leu Phe Thr Glu Val Met
 1

48

25

30

55 GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Thr Thr Thr Thr Thr

111

92

	35	40	45	
5	TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr	192		
	50	55	60	
10	CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys	240		
	65	70	75	80
15	CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu	288		
	85	90	95	
20	CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu	336		
	100	105	110	
25	GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly	384		
	115	120	125	
30	ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr	432		
	130	135	140	
35	AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn	480		
	145	150	155	160
40	GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser	528		
	165	170	175	
45	GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly	576		
	180	185	190	
50	CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu	624		
	195	200	205	
55	AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe	672		
	210	215	220	
60	GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Gln Thr Thr Thr Thr	720		
	225			
65				
70				
75				
80				
85				
90				
95				
100				
105				
110				
115				
120				
125				
130				
135				
140				
145				
150				
155				
160				
165				
170				
175				
180				
185				
190				
195				
200				
205				
210				
215				
220				
225				
230				
235				
240				
245				
250				
255				
260				
265				
270				
275				
280				
285				
290				
295				
300				
305				
310				
315				
320				
325				
330				
335				
340				
345				
350				
355				
360				
365				
370				
375				
380				
385				
390				
395				
400				
405				
410				
415				
420				
425				
430				
435				
440				
445				
450				
455				
460				
465				
470				
475				
480				
485				
490				
495				
500				
505				
510				
515				
520				
525				
530				
535				
540				
545				
550				
555				
560				
565				
570				
575				
580				
585				
590				
595				
600				
605				
610				
615				
620				
625				
630				
635				
640				
645				
650				
655				
660				
665				
670				
675				
680				
685				
690				
695				
700				
705				
710				
715				
720				
725				
730				
735				
740				
745				
750				
755				
760				
765				
770				
775				
780				
785				
790				
795				
800				
805				
810				
815				
820				
825				
830				
835				
840				
845				
850				
855				
860				
865				
870				
875				
880				
885				
890				
895				
900				
905				
910				
915				
920				
925				
930				
935				
940				
945				
950				
955				
960				
965				
970				
975				
980				
985				
990				
995				

93

	260	265	270	
5	ATA TTG ACT GTG AAT AAA GGG TCC TTA GTA GCT CTT GGA TTC AGT GAT Ile Leu Thr Val Asn Lys Gly Ser Leu Val Ala Leu Gly Phe Ser Asp 275 280 285	864		
10	GGA CAG GAA GCC AGG CCT GAA GAA ATT GGC TGG TTA AAT GGC TAT AAT Gly Gln Glu Ala Arg Pro Glu Glu Ile Gly Trp Leu Asn Gly Tyr Asn 290 295 300	912		
15	GAA ACC ACA GGG GAA AGG GGG GAC TTT CCG GGA ACT TAC GTA GAA TAT Glu Thr Thr Gly Glu Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Tyr 305 310 315 320	960		
20	ATT GGA AGG AAA AAA ATC TCG CCT CCC ACA CCA AAG CCC CGG CCA CCT Ile Gly Arg Lys Lys Ile Ser Pro Pro Thr Pro Lys Pro Arg Pro Pro 325 330 335	1008		
25	CGG CCT CTT CCT GTT GCA CCA GGT TCT TCG AAA ACT GAA GCA GAT GTT Arg Pro Leu Pro Val Ala Pro Gly Ser Ser Lys Thr Glu Ala Asp Val 340 345 350	1056		
30	GAA CAA CAA GCT TTG ACT CTC CCG GAT CTT GCA GAG CAG TTT GCC CCT Glu Gln Gln Ala Leu Thr Leu Pro Asp Leu Ala Glu Gln Phe Ala Pro 355 360 365	1104		
35	CCT GAC ATT GCC CCG CCT CTT CTT ATC AAG CTC GTG GAA GCC ATT GAA Pro Asp Ile Ala Pro Pro Leu Leu Ile Lys Leu Val Glu Ala Ile Glu 370 375 380	1152		
40	AAG AAA GGT CTG GAA TGT TCA ACT CTA TAC AGA ACA CAG AGC TCC AGC Lys Lys Gly Leu Glu Cys Ser Thr Leu Tyr Arg Thr Gln Ser Ser Ser 385 390 395 400	1200		
45	AAC CTG GCA GAA TTA CGA CAG CTT CTT GAT TGT GAT ACA CCC TCC GTG Asn Leu Ala Glu Leu Arg Gln Leu Leu Asp Cys Asp Thr Pro Ser Val 405 410 415	1248		
50	GAC TTG GAA ATG ATC GAT GTG CAC GTT TTG GCT GAC GCT TTC AAA CGC Asp Leu Glu Met Ile Asp Val His Val Leu Ala Asp Ala Phe Lys Arg 420 425 430	1296		
55	TAT CTC CTG GAC TTA CCA AAT CCT GTC ATT CCA GCA GCC GTT TAC AGT Tyr Leu Leu Asp Leu Pro Asn Pro Val Ile Pro Ala Ala Val Tyr Ser 435 440 445	1344		
60	GAA ATG ATT TCT TTA GCT CCA GAA GTA CAA AGC TCC GAA GAA TAT ATT Glu Met Ile Ser Leu Ala Pro Glu Val Gln Ser Ser Ser Ser 450 455 460 465 470 475 480	1392		
65	TGG CTT ACG CTT CAG TAT TTG TTA AAA CAT TTC TTC AAG CTC TCT GAA Trp Leu Thr Leu Gln Tyr Leu Leu Leu Leu Leu Leu Leu Leu Leu Leu 485 490 495 500 505 510 515 520 525 530 535 540	1440		

94

	485								490				495					
5	ACC	TCC	AGC	AAA	AAT	CTG	TTG	AAT	GCA	AGA	GTA	CTC	TCT	GAA	ATT	TTC	1536	
	Thr	Ser	Ser	Lys	Asn	Leu	Leu	Asn	Ala	Arg	Val	Leu	Ser	Glu	Ile	Phe		
				500					505					510				
10	AGC	CCT	ATG	CTT	TTC	AGA	TTC	TCA	GCA	GCC	AGC	TCT	GAT	AAT	ACT	GAA	1584	
	Ser	Pro	Met	Leu	Phe	Arg	Phe	Ser	Ala	Ala	Ser	Ser	Asp	Asn	Thr	Glu		
			515					520					525					
15	AAC	CTC	ATA	AAA	GTT	ATA	GAA	ATT	TTA	ATC	TCA	ACT	GAA	TGG	AAT	GAA	1632	
	Asn	Leu	Ile	Lys	Val	Ile	Glu	Ile	Leu	Ile	Ser	Thr	Glu	Trp	Asn	Glu		
			530				535					540						
20	CGA	CAG	CCT	GCA	CCA	GCA	CTG	CCT	CCT	AAA	CCA	CCA	AAA	CCT	ACT	ACT	1680	
	Arg	Gln	Pro	Ala	Pro	Ala	Leu	Pro	Pro	Lys	Pro	Pro	Lys	Pro	Thr	Thr		
	545					550					555					560		
25	GTA	GCC	AAC	AAC	GGT	ATG	AAT	AAC	AAT	ATG	TCC	TTA	CAA	AAT	GCT	GAA	1728	
	Val	Ala	Asn	Asn	Gly	Met	Asn	Asn	Asn	Met	Ser	Leu	Gln	Asn	Ala	Glu		
					565					570					575			
30	TGG	TAC	TGG	GGA	GAT	ATC	TCG	AGG	GAA	GAA	GTG	AAT	GAA	AAA	CTT	CGA	1776	
	Trp	Tyr	Trp	Gly	Asp	Ile	Ser	Arg	Glu	Glu	Val	Asn	Glu	Lys	Leu	Arg		
				580					585					590				
35	GAT	ACA	GCA	GAC	GGG	ACC	TTT	TTG	GTA	CGA	GAT	GCG	TCT	ACT	AAA	ATG	1824	
	Asp	Thr	Ala	Asp	Gly	Thr	Phe	Leu	Val	Arg	Asp	Ala	Ser	Thr	Lys	Met		
			595					600					605					
40	CAT	GGT	GAT	TAT	ACT	CTT	ACA	CTA	AGG	AAA	GGG	GGA	AAT	AAC	AAA	TTA	1872	
	His	Gly	Asp	Tyr	Thr	Leu	Thr	Leu	Arg	Lys	Gly	Gly	Asn	Asn	Lys	Leu		
		610					615					620						
45	ATC	AAA	ATA	TTT	CAT	CGA	GAT	GGG	AAA	TAT	GGC	TTC	TCT	GAC	CCA	TTA	1920	
	Ile	Lys	Ile	Phe	His	Arg	Asp	Gly	Lys	Tyr	Gly	Phe	Ser	Asp	Pro	Leu		
	625					630					635				640			
50	ACC	TTC	AGT	TCT	GTG	GTT	GAA	TTA	ATA	AAC	CAC	TAC	CGG	AAT	GAA	TCT	1968	
	Thr	Phe	Ser	Ser	Val	Val	Glu	Leu	Ile	Asn	His	Tyr	Arg	Asn	Glu	Ser		
					645					650					655			
55	CTA	GCT	CAG	TAT	AAT	CCC	AAA	TTG	GAT	GTG	AAA	TTA	CTT	TAT	CCA	GTA	2016	
	Leu	Ala	Gln	Tyr	Asn	Pro	Lys	Leu	Asp	Val	Lys	Leu	Leu	Tyr	Pro	Val		
				660				665					670					
60	TCC	AAA	TAC	CAA	CAG	GAT	CAA	GTT	GTC	AAA	GAA	GAT	AAT	ATT	GAA	GCT	2064	
	Ser	Lys	Tyr	Gln	Gln	Asp	Gln	Val	Val	Lys	Glu	Leu	Leu	Leu	Leu	Leu		
				675														
65	CGA	GAA	TAT	GAT	AGA	TTA	TAT	GAA	GAA	TAT	ACC	CGC	ACA	TCC	CAG	GAA	2112	
	Arg	Glu	Tyr	Asp	Arg	Leu	Tyr	Glu	Glu	Thr	Thr	Thr	Thr	Thr	Thr	Thr		

95																	
705				710				715				720					
5	ATC	CAA	ATG	AAA	AGG	ACA	GCT	ATT	GAA	GCA	TTT	AAT	GAA	ACC	ATA	AAA	2208
	Ile	Gln	Met	Lys	Arg	Thr	Ala	Ile	Glu	Ala	Phe	Asn	Glu	Thr	Ile	Lys	
	725				730				735								
10	ATA	TTT	GAA	GAA	CAG	TGC	CAG	ACC	CAA	GAG	CGG	TAC	AGC	AAA	GAA	TAC	2256
	Ile	Phe	Glu	Glu	Gln	Cys	Gln	Thr	Gln	Glu	Arg	Tyr	Ser	Lys	Glu	Tyr	
	740				745				750								
15	ATA	GAA	AAG	TTT	AAA	CGT	GAA	GGC	AAT	GAG	AAA	GAA	ATA	CAA	AGG	ATT	2304
	Ile	Glu	Lys	Phe	Lys	Arg	Glu	Gly	Asn	Glu	Lys	Glu	Ile	Gln	Arg	Ile	
	755				760				765								
20	ATG	CAT	AAT	TAT	GAT	AAG	TTG	AAG	TCT	CGA	ATC	AGT	GAA	ATT	ATT	GAC	2352
	Met	His	Asn	Tyr	Asp	Lys	Leu	Lys	Ser	Arg	Ile	Ser	Glu	Ile	Ile	Asp	
	770				775				780								
25	AGT	AGA	AGA	AGA	TTG	GAA	GAA	GAC	TTG	AAG	AAG	CAG	GCA	GCT	GAG	TAT	2400
	Ser	Arg	Arg	Arg	Leu	Glu	Glu	Asp	Leu	Lys	Lys	Gln	Ala	Ala	Glu	Tyr	
	785				790				795				800				
30	CGA	GAA	ATT	GAC	AAA	CGT	ATG	AAC	AGC	ATT	AAA	CCA	GAC	CTT	ATC	CAG	2448
	Arg	Glu	Ile	Asp	Lys	Arg	Met	Asn	Ser	Ile	Lys	Pro	Asp	Leu	Ile	Gln	
	805				810				815								
35	CTG	AGA	AAG	ACG	AGA	GAC	CAA	TAC	TTG	ATG	TGG	TTG	ACT	CAA	AAA	GGT	2496
	Leu	Arg	Lys	Thr	Arg	Asp	Gln	Tyr	Leu	Met	Trp	Leu	Thr	Gln	Lys	Gly	
	820				825				830								
40	GTT	CGG	CAA	AAG	AAG	TTG	AAC	GAG	TGG	TTG	GGC	AAT	GAA	AAC	ACT	GAA	2544
	Val	Arg	Gln	Lys	Lys	Leu	Asn	Glu	Trp	Leu	Gly	Asn	Glu	Asn	Thr	Glu	
	835				840				845								
45	GAC	CAA	TAT	TCA	CTG	GTG	GAA	GAT	GAT	GAA	GAT	TTG	CCC	CAT	CAT	GAT	2592
	Asp	Gln	Tyr	Ser	Leu	Val	Glu	Asp	Asp	Glu	Asp	Leu	Pro	His	His	Asp	
	850				855				860								
50	GAG	AAG	ACA	TGG	AAT	GTT	GGA	AGC	AGC	AAC	CGA	AAC	AAA	GCT	GAA	AAC	2640
	Glu	Lys	Thr	Trp	Asn	Val	Gly	Ser	Ser	Asn	Arg	Asn	Lys	Ala	Glu	Asn	
	865				870				875				880				
55	CTG	TTG	CGA	GGG	AAG	CGA	GAT	GGC	ACT	TTT	CTT	GTC	CGG	GAG	AGC	AGT	2688
	Leu	Leu	Arg	Gly	Lys	Arg	Asp	Gly	Thr	Phe	Leu	Val	Arg	Glu	Ser	Ser	
	885				890				895								
60	AAA	CAG	GGC	TGC	TAT	GCC	TGC	TCT	GTA	GTG	GTG	GAC	GGC	GAA	GTA	AAG	2736
	Lys	Gln	Gly	Cys	Tyr	Ala	Cys	Ser	Val	Val	Val	Asp	Val	Val	Val	Val	
	900				905				910				915				
65	TAT	AAC	TTG	TAC	AGC	TCT	CTG	AAA	GAA	CTG	GTG	CTA	CAT	TAC	CAA	CAG	2880
	Tyr	Asn	Leu	Tyr	Ser	Ser	Leu	Lys	Gln	Leu	Val	Val	Val	Val	Val	Val	
	920				925				930				935				

96

[illegible]

(2) INFORMATION FOR SEO ID NO:49:

(i) SEQUENCE CHARACTERISTICS:

- 15 (A) LENGTH: 968 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

[illegible]

55 Gly Leu Arg Ser Met Ser Ala Glu Gly Tyr Gln Tyr Arg Ala Leu Tyr

	Asp	Tyr	Lys	Lys	Glu	Arg	Glu	Glu	Asp	Ile	Asp	Leu	His	Leu	Gly	Asp
				260					265					270		
	Ile	Leu	Thr	Val	Asn	Lys	Gly	Ser	Leu	Val	Ala	Leu	Gly	Phe	Ser	Asp
				275					280					285		
5	Gly	Gln	Glu	Ala	Arg	Pro	Glu	Glu	Ile	Gly	Trp	Leu	Asn	Gly	Tyr	Asn
				290					295					300		
	Glu	Thr	Thr	Gly	Glu	Arg	Gly	Asp	Phe	Pro	Gly	Thr	Tyr	Val	Glu	Tyr
																320
	Ile	Gly	Arg	Lys	Lys	Ile	Ser	Pro	Pro	Thr	Pro	Lys	Pro	Arg	Pro	Pro
																335
10	Arg	Pro	Leu	Pro	Val	Ala	Pro	Gly	Ser	Ser	Lys	Thr	Glu	Ala	Asp	Val
																350
	Glu	Gln	Gln	Ala	Leu	Thr	Leu	Pro	Asp	Leu	Ala	Glu	Gln	Phe	Ala	Pro
																365
15	Pro	Asp	Ile	Ala	Pro	Pro	Leu	Leu	Ile	Lys	Leu	Val	Glu	Ala	Ile	Glu
																380
	Lys	Lys	Gly	Leu	Glu	Cys	Ser	Thr	Leu	Tyr	Arg	Thr	Gln	Ser	Ser	Ser
																400
	Asn	Leu	Ala	Glu	Leu	Arg	Gln	Leu	Leu	Asp	Cys	Asp	Thr	Pro	Ser	Val
																415
20	Asp	Leu	Glu	Met	Ile	Asp	Val	His	Val	Leu	Ala	Asp	Ala	Phe	Lys	Arg
																430
	Tyr	Leu	Leu	Asp	Leu	Pro	Asn	Pro	Val	Ile	Pro	Ala	Ala	Val	Tyr	Ser
																445
25	Glu	Met	Ile	Ser	Leu	Ala	Pro	Glu	Val	Gln	Ser	Ser	Glu	Glu	Tyr	Ile
																460
	Gln	Leu	Leu	Lys	Lys	Leu	Ile	Arg	Ser	Pro	Ser	Ile	Pro	His	Gln	Tyr
																480
	Trp	Leu	Thr	Leu	Gln	Tyr	Leu	Leu	Lys	His	Phe	Phe	Lys	Leu	Ser	Gln
																495
30	Thr	Ser	Ser	Lys	Asn	Leu	Leu	Asn	Ala	Arg	Val	Leu	Ser	Glu	Ile	Phe
																510
	Ser	Pro	Met	Leu	Phe	Arg	Phe	Ser	Ala	Ala	Ser	Ser	Asp	Asn	Thr	Glu
																525
35	Asn	Leu	Ile	Lys	Val	Ile	Glu	Ile	Leu	Ile	Ser	Thr	Glu	Trp	Asn	Glu
																540
	Arg	Gln	Pro	Ala	Pro	Ala	Leu	Pro	Pro	Lys	Pro	Pro	Lys	Pro	Thr	Thr
																560
40	Val	Ala	Asn	Asn	Gly	Met	Asn	Asn	Asn	Met	Ser	Leu	Gln	Asn	Ala	Glu
																575
	Trp	Tyr	Trp	Gly	Asp	Ile	Ser	Arg	Glu	Glu	Val	Asn	Glu	Lys	Leu	Arg
																590
	Asp	Thr	Ala	Asp	Gly	Thr	Phe	Leu	Val	Arg						

98

Arg Glu Tyr Asp Arg Leu Tyr Glu Glu Tyr Thr Arg Thr Ser Gln Glu
 705 710 715 720
 Ile Gln Met Lys Arg Thr Ala Ile Glu Ala Phe Asn Glu Thr Ile Lys
 725 730 735
 5 Ile Phe Glu Glu Gln Cys Gln Thr Gln Glu Arg Tyr Ser Lys Glu Tyr
 740 745 750
 Ile Glu Lys Phe Lys Arg Glu Gly Asn Glu Lys Glu Ile Gln Arg Ile
 755 760 765
 10 Met His Asn Tyr Asp Lys Leu Lys Ser Arg Ile Ser Glu Ile Ile Asp
 770 775 780
 Ser Arg Arg Arg Leu Glu Glu Asp Leu Lys Lys Gln Ala Ala Glu Tyr
 785 790 795 800
 Arg Glu Ile Asp Lys Arg Met Asn Ser Ile Lys Pro Asp Leu Ile Gln
 805 810 815
 15 Leu Arg Lys Thr Arg Asp Gln Tyr Leu Met Trp Leu Thr Gln Lys Gly
 820 825 830
 Val Arg Gln Lys Lys Leu Asn Glu Trp Leu Gly Asn Glu Asn Thr Glu
 835 840 845
 20 Asp Gln Tyr Ser Leu Val Glu Asp Asp Glu Asp Leu Pro His His Asp
 850 855 860
 Glu Lys Thr Trp Asn Val Gly Ser Ser Asn Arg Asn Lys Ala Glu Asn
 865 870 875 880
 Leu Leu Arg Gly Lys Arg Asp Gly Thr Phe Leu Val Arg Glu Ser Ser
 885 890 895
 25 Lys Gln Gly Cys Tyr Ala Cys Ser Val Val Val Asp Gly Glu Val Lys
 900 905 910
 His Cys Val Ile Asn Lys Thr Ala Thr Gly Tyr Gly Phe Ala Glu Pro
 915 920 925
 30 Tyr Asn Leu Tyr Ser Ser Leu Lys Glu Leu Val Leu His Tyr Gln His
 930 935 940
 Thr Ser Leu Val Gln His Asn Asp Ser Leu Asn Val Thr Leu Ala Tyr
 945 950 955 960
 Pro Val Tyr Ala Gln Gln Arg Arg
 965

35

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 2160 base pairs
 40 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
 45 (ix) FEATURE:

(A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...2157

55 Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1 5 10 15

48

99

	GTC	GAG	CTG	GAC	GGC	GAC	GTA	AAC	GGC	CAC	AAG	TTC	AGC	GTG	TCC	GGC	96
	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	
				20					25					30			
5	GAG	GGC	GAG	GGC	GAT	GCC	ACC	TAC	GGC	AAG	CTG	ACC	CTG	AAG	TTC	ATC	144
	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	
			35					40					45				
10	TGC	ACC	ACC	GGC	AAG	CTG	CCC	GTG	CCC	TGG	CCC	ACC	CTC	GTG	ACC	ACC	192
	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	
		50					55					60					
15	CTG	ACC	TAC	GGC	GTG	CAG	TGC	TTC	AGC	CGC	TAC	CCC	GAC	CAC	ATG	AAG	240
	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	
	65					70				75						80	
20	CAG	CAC	GAC	TTC	TTC	AAG	TCC	GCC	ATG	CCC	GAA	GGC	TAC	GTG	CAG	GAG	288
	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	
				85						90					95		
25	CGC	ACC	ATC	TTC	TTC	AAG	GAC	GAC	GGC	AAC	TAC	AAG	ACC	CGC	GCC	GAG	336
	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	
				100					105					110			
30	ATC	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	CAC	AAG	CTG	GAG	TAC	432
	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	
		130					135					140					
35	AAC	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	GAC	AAG	CAG	AAG	AAC	480
	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	
	145					150					155					160	
40	GGC	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	ATC	GAG	GAC	GGC	AGC	528
	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	
				165					170						175		
45	GTG	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	CCC	ATC	GGC	GAC	GGC	576
	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	
				180					185					190			
50	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	ACC	CAG	TCC	GCC	CTG	624
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	
			195				200						205				
55	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser	720
	225					230					235						

100																	
	GGA	CTC	AGA	TCT	CGA	GCT	CAA	GCT	TCG	AAT	TCG	ACC	ATG	TCG	TCC	ATC	768
	Gly	Leu	Arg	Ser	Arg	Ala	Gln	Ala	Ser	Asn	Ser	Thr	Met	Ser	Ser	Ile	
					245					250					255		
5	TTG	CCA	TTC	ACG	CCG	CCA	GTT	GTG	AAG	AGA	CTG	CTG	GGA	TGG	AAG	AAG	816
	Leu	Pro	Phe	Thr	Pro	Pro	Val	Val	Lys	Arg	Leu	Leu	Gly	Trp	Lys	Lys	
				260					265					270			
10	TCA	GCT	GGT	GGG	TCT	GGA	GGA	GCA	GGC	GGA	GGA	GAG	CAG	AAT	GGG	CAG	864
	Ser	Ala	Gly	Gly	Ser	Gly	Gly	Ala	Gly	Gly	Gly	Glu	Gln	Asn	Gly	Gln	
			275					280					285				
15	GAA	GAA	AAG	TGG	TGT	GAG	AAA	GCA	GTG	AAA	AGT	CTG	GTG	AAG	AAG	CTA	912
	Glu	Glu	Lys	Trp	Cys	Glu	Lys	Ala	Val	Lys	Ser	Leu	Val	Lys	Lys	Leu	
		290					295					300					
20	AAG	AAA	ACA	GGA	CGA	TTA	GAT	GAG	CTT	GAG	AAA	GCC	ATC	ACC	ACT	CAA	960
	Lys	Lys	Thr	Gly	Arg	Leu	Asp	Glu	Leu	Glu	Lys	Ala	Ile	Thr	Thr	Gln	
	305					310					315					320	
	AAC	TGT	AAT	ACT	AAA	TGT	GTT	ACC	ATA	CCA	AGC	ACT	TGC	TCT	GAA	ATT	1008
	Asn	Cys	Asn	Thr	Lys	Cys	Val	Thr	Ile	Pro	Ser	Thr	Cys	Ser	Glu	Ile	
					325					330					335		
25	TGG	GGA	CTG	AGT	ACA	CCA	AAT	ACG	ATA	GAT	CAG	TGG	GAT	ACA	ACA	GGC	1056
	Trp	Gly	Leu	Ser	Thr	Pro	Asn	Thr	Ile	Asp	Gln	Trp	Asp	Thr	Thr	Gly	
				340					345					350			
30	CTT	TAC	AGC	TTC	TCT	GAA	CAA	ACC	AGG	TCT	CTT	GAT	GGT	CGT	CTC	CAG	1104
	Leu	Tyr	Ser	Phe	Ser	Glu	Gln	Thr	Arg	Ser	Leu	Asp	Gly	Arg	Leu	Gln	
			355					360					365				
35	GTA	TCC	CAT	CGA	AAA	GGA	TTG	CCA	CAT	GTT	ATA	TAT	TGC	CGA	TTA	TGG	1152
	Val	Ser	His	Arg	Lys	Gly	Leu	Pro	His	Val	Ile	Tyr	Cys	Arg	Leu	Trp	
		370					375					380					
40	CGC	TGG	CCT	GAT	CTT	CAC	AGT	CAT	CAT	GAA	CTC	AAG	GCA	ATT	GAA	AAC	1200
	Arg	Trp	Pro	Asp	Leu	His	Ser	His	His	Glu	Leu	Lys	Ala	Ile	Glu	Asn	
	385					390					395				400		
	TGC	GAA	TAT	GCT	TTT	AAT	CTT	AAA	AAG	GAT	GAA	GTA	TGT	GTA	AAC	CCT	1248
	Cys	Glu	Tyr	Ala	Phe	Asn	Leu	Lys	Lys	Asp	Glu	Val	Cys	Val	Asn	Pro	
				405						410					415		
45	TAC	CAC	TAT	CAG	AGA	GTT	GAG	ACA	CCA	GTT	TTG	CCT	CCA	GTA	TTA	GTG	1296
	Tyr	His	Tyr	Gln	Arg	Val	Glu	Thr	Pro	Val	Leu	Pro	Pro	Val	Leu	Val	
				420					425					430			
100																	
55	TTT	AAA	TCC	ATT	CGA	GAA	AAC	ACT	AAC	TTC	CCA	GCA	GGA	ATT	GAG	CCA	1392
	Thr	His	Ser	Ile	Pro	Glu	Asn	Thr	Asn	Phe	Pro	Ala	Gly	Ile	Glu	Pro	
		450					455					460					

101

	CAG AGT AAT TAT ATT CCA GAA ACG CCA CCT CCT GGA TAT ATC AGT GAA	1440
	Gln Ser Asn Tyr Ile Pro Glu Thr Pro Pro Pro Gly Tyr Ile Ser Glu	
	465 470 475 480	
5	GAT GGA GAA ACA AGT GAC CAA CAG TTG AAT CAA AGT ATG GAC ACA GGC	1488
	Asp Gly Glu Thr Ser Asp Gln Gln Leu Asn Gln Ser Met Asp Thr Gly	
	485 490 495	
10	TCT CCA GCA GAA CTA TCT CCT ACT ACT CTT TCC CCT GTT AAT CAT AGC	1536
	Ser Pro Ala Glu Leu Ser Pro Thr Thr Leu Ser Pro Val Asn His Ser	
	500 505 510	
15	TTG GAT TTA CAG CCA GTT ACT TAC TCA GAA CCT GCA TTT TGG TGT TCA	1584
	Leu Asp Leu Gln Pro Val Thr Tyr Ser Glu Pro Ala Phe Trp Cys Ser	
	515 520 525	
20	ATA GCA TAT TAT GAA TTA AAT CAG AGG GTT GGA GAA ACC TTC CAT GCA	1632
	Ile Ala Tyr Tyr Glu Leu Asn Gln Arg Val Gly Glu Thr Phe His Ala	
	530 535 540	
25	TCA CAG CCC TCA CTC ACT GTA GAT GGC TTT ACA GAC CCA TCA AAT TCA	1680
	Ser Gln Pro Ser Leu Thr Val Asp Gly Phe Thr Asp Pro Ser Asn Ser	
	545 550 555 560	
30	GAG AGG TTC TGC TTA GGT TTA CTC TCC AAT GTT AAC CGA AAT GCC ACG	1728
	Glu Arg Phe Cys Leu Gly Leu Leu Ser Asn Val Asn Arg Asn Ala Thr	
	565 570 575	
35	GTA GAA ATG ACA AGA AGG CAT ATA GGA AGA GGA GTG CGC TTA TAC TAC	1776
	Val Glu Met Thr Arg Arg His Ile Gly Arg Gly Val Arg Leu Tyr Tyr	
	580 585 590	
40	ATA GGT GGG GAA GTT TTT GCT GAG TGC CTA AGT GAT AGT GCA ATC TTT	1824
	Ile Gly Gly Glu Val Phe Ala Glu Cys Leu Ser Asp Ser Ala Ile Phe	
	595 600 605	
45	GTG CAG AGC CCC AAT TGT AAT CAG AGA TAT GGC TGG CAC CCT GCA ACA	1872
	Val Gln Ser Pro Asn Cys Asn Gln Arg Tyr Gly Trp His Pro Ala Thr	
	610 615 620	
50	GTG TGT AAA ATT CCA CCA GGC TGT AAT CTG AAG ATC TTC AAC AAC CAG	1920
	Val Cys Lys Ile Pro Pro Gly Cys Asn Leu Lys Ile Phe Asn Asn Gln	
	625 630 635 640	
55	GAA TTT GCT GCT CTT CTG GCT CAG TCT GTT AAT CAG GGT TTT GAA GCC	1968
	Glu Phe Ala Ala Leu Leu Ala Gln Ser Val Asn Gln Gly Phe Glu Ala	
	645 650 655	
60	GTC GAT GAG GAA TAC CCA AGG CAG ACG GTA ACA AGT ACT CCT TGC	2064
	Gly Trp Gly Ala Glu Tyr Arg Arg Gln Thr Val Thr Ser Thr Pro Cys	
	675 680 685	

102

TGG ATT GAA CTT CAT CTG AAT GGA CCT CTA CAG TGG TTG GAC AAA GTA 2112
 Trp Ile Glu Leu His Leu Asn Gly Pro Leu Gln Trp Leu Asp Lys Val
 690 695 700

5 TTA ACT CAG ATG GGA TCC CCT TCA GTG CGT TGC TCA AGC ATG TCA TAA 2160
 Leu Thr Gln Met Gly Ser Pro Ser Val Arg Cys Ser Ser Met Ser
 705 710 715

10 (2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 719 amino acids

(B) TYPE: amino acid

15 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1 5 10 15
 25 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
 20 25 30
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
 35 40 45
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 50 55 60
 30 Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
 65 70 75 80
 Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
 85 90 95
 35 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
 100 105 110
 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
 115 120 125
 Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
 130 135 140
 40 Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
 145 150 155 160
 Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
 165 170 175
 45 Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
 180 185 190
 Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
 195 200
 240
 245 250 255
 55 Leu Pro Phe Thr Pro Pro Val Val Lys Arg Leu Leu Gly Trp Lys Lys
 260

103

	Ser	Ala	Gly	Gly	Ser	Gly	Gly	Ala	Gly	Gly	Gly	Glu	Gln	Asn	Gly	Gln
		275						280					285			
	Glu	Glu	Lys	Trp	Cys	Glu	Lys	Ala	Val	Lys	Ser	Leu	Val	Lys	Lys	Leu
		290					295					300				
5	Lys	Lys	Thr	Gly	Arg	Leu	Asp	Glu	Leu	Glu	Lys	Ala	Ile	Thr	Thr	Gln
	305					310					315					320
	Asn	Cys	Asn	Thr	Lys	Cys	Val	Thr	Ile	Pro	Ser	Thr	Cys	Ser	Glu	Ile
					325					330					335	
10	Trp	Gly	Leu	Ser	Thr	Pro	Asn	Thr	Ile	Asp	Gln	Trp	Asp	Thr	Thr	Gly
				340					345					350		
	Leu	Tyr	Ser	Phe	Ser	Glu	Gln	Thr	Arg	Ser	Leu	Asp	Gly	Arg	Leu	Gln
		355						360					365			
	Val	Ser	His	Arg	Lys	Gly	Leu	Pro	His	Val	Ile	Tyr	Cys	Arg	Leu	Trp
	370						375					380				
15	Arg	Trp	Pro	Asp	Leu	His	Ser	His	His	Glu	Leu	Lys	Ala	Ile	Glu	Asn
	385					390					395					400
	Cys	Glu	Tyr	Ala	Phe	Asn	Leu	Lys	Lys	Asp	Glu	Val	Cys	Val	Asn	Pro
				405						410					415	
20	Tyr	His	Tyr	Gln	Arg	Val	Glu	Thr	Pro	Val	Leu	Pro	Pro	Val	Leu	Val
				420					425					430		
	Pro	Arg	His	Thr	Glu	Ile	Leu	Thr	Glu	Leu	Pro	Pro	Leu	Asp	Asp	Tyr
		435						440					445			
	Thr	His	Ser	Ile	Pro	Glu	Asn	Thr	Asn	Phe	Pro	Ala	Gly	Ile	Glu	Pro
	450						455					460				
25	Gln	Ser	Asn	Tyr	Ile	Pro	Glu	Thr	Pro	Pro	Pro	Gly	Tyr	Ile	Ser	Glu
	465					470					475					480
	Asp	Gly	Glu	Thr	Ser	Asp	Gln	Gln	Leu	Asn	Gln	Ser	Met	Asp	Thr	Gly
				485						490					495	
30	Ser	Pro	Ala	Glu	Leu	Ser	Pro	Thr	Thr	Leu	Ser	Pro	Val	Asn	His	Ser
			500						505					510		
	Leu	Asp	Leu	Gln	Pro	Val	Thr	Tyr	Ser	Glu	Pro	Ala	Phe	Trp	Cys	Ser
		515						520					525			
	Ile	Ala	Tyr	Tyr	Glu	Leu	Asn	Gln	Arg	Val	Gly	Glu	Thr	Phe	His	Ala
	530						535					540				
35	Ser	Gln	Pro	Ser	Leu	Thr	Val	Asp	Gly	Phe	Thr	Asp	Pro	Ser	Asn	Ser
	545					550					555					560
	Glu	Arg	Phe	Cys	Leu	Gly	Leu	Leu	Ser	Asn	Val	Asn	Arg	Asn	Ala	Thr
				565						570					575	
40	Val	Glu	Met	Thr	Arg	Arg	His	Ile	Gly	Arg	Gly	Val	Arg	Leu	Tyr	Tyr
				580					585					590		
	Ile	Gly	Gly	Glu	Val	Phe	Ala	Glu	Cys	Leu	Ser	Asp	Ser	Ala	Ile	Phe
		595						600					605			
	Val	Gln	Ser	Pro	Asn	Cys	Asn	Gln	Arg	Tyr	Gly	Trp	His	Pro	Ala	Thr
	610						615					620				
45	Val	Cys	Lys	Ile	Pro	Pro	Gly	Cys	Asn	Leu	Lys	Ile	Phe	Asn	Asn	Gln
	625					630					635					640
	Glu	Phe	Ala	Ala	Leu	Leu	Ala	Gln	Ser	Val	Asn	Gln	Gly	Phe	Glu	Ala
				645						650						
	Val	Thr	Gln	Met	Gly	Ser	Pro	Ser	Val	Arg	Cys	Ser	Ser	Met	Ser	
55																
	690					695					700					
	Leu	Thr	Gln	Met	Gly	Ser	Pro	Ser	Val	Arg	Cys	Ser	Ser	Met	Ser	
	705					710										

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 2421 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2418
15 (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

20	ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG	48
	Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu	
	1 5 10 15	
25	GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC	96
	Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly	
	20 25 30	
30	GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC	144
	Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile	
	35 40 45	
35	TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC	192
	Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr	
	50 55 60	
40	CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG	240
	Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys	
	65 70 75 80	
45	CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG	288
	Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu	
	85 90 95	
50	CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG	336
	Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu	
	100 105 110	
55	GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC	384
	Val Lys Phe Glu Gly Asp Thr Leu Val Thr Thr Thr Thr Thr Thr Thr	
	115 120 125 130 135 140	
60	AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC	432
	Asn Tyr Asn Ser His Asn Val Thr Thr Thr Thr Thr Thr Thr Thr Thr	

105																			
145					150					155					160				
5	GGC	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	ATC	GAG	GAC	GGC	AGC	528		
	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser			
					165								175						
10	GTG	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	CCC	ATC	GGC	GAC	GGC	576		
	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly			
					180								190						
15	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	ACC	CAG	TCC	GCC	CTG	624		
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu			
					195								205						
20	AGC	AAA	GAC	CCC	AAC	GAG	AAG	CGC	GAT	CAC	ATG	GTC	CTG	CTG	GAG	TTC	672		
	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe			
					210								220						
25	GTG	ACC	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	GAG	CTG	TAC	AAG	TCC	720		
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser			
					225								235				240		
30	GGA	CTC	AGA	TCT	CGA	GCT	CAA	GCT	TCG	AAT	TCG	AAT	TCA	ACC	ATG	GAC	768		
	Gly	Leu	Arg	Ser	Arg	Ala	Gln	Ala	Ser	Asn	Ser	Asn	Ser	Thr	Met	Asp			
					245								255						
35	AAT	ATG	TCT	ATT	ACG	AAT	ACA	CCA	ACA	AGT	AAT	GAT	GCC	TGT	CTG	AGC	816		
	Asn	Met	Ser	Ile	Thr	Asn	Thr	Pro	Thr	Ser	Asn	Asp	Ala	Cys	Leu	Ser			
					260								270						
40	ATT	GTG	CAT	AGT	TTG	ATG	TGC	CAT	AGA	CAA	GGT	GGA	GAG	AGT	GAA	ACA	864		
	Ile	Val	His	Ser	Leu	Met	Cys	His	Arg	Gln	Gly	Gly	Glu	Ser	Glu	Thr			
					275								285						
45	TTT	GCA	AAA	AGA	GCA	ATT	GAA	AGT	TTG	GTA	AAG	AAG	CTG	AAG	GAG	AAA	912		
	Phe	Ala	Lys	Arg	Ala	Ile	Glu	Ser	Leu	Val	Lys	Lys	Leu	Lys	Glu	Lys			
					290								300						
50	AAA	GAT	GAA	TTG	GAT	TCT	TTA	ATA	ACA	GCT	ATA	ACT	ACA	AAT	GGA	GCT	960		
	Lys	Asp	Glu	Leu	Asp	Ser	Leu	Ile	Thr	Ala	Ile	Thr	Thr	Asn	Gly	Ala			
					305								315				320		
55	CAT	CCT	AGT	AAA	TGT	GTT	ACC	ATA	CAG	AGA	ACA	TTG	GAT	GGG	AGG	CTT	1008		
	His	Pro	Ser	Lys	Cys	Val	Thr	Ile	Gln	Arg	Thr	Leu	Asp	Gly	Arg	Leu			
					325								335						
60	CAG	GTG	GCT	GGT	CGG	AAA	GGA	TTT	CCT	CAT	GTG	ATC	TAT	GCC	CGT	CTC	1056		
	Gln	Val	Ala	Gly	Arg	Ile	Gly	Phe	Thr	Val	Leu	Val	Leu	Val	Leu	Val			
					340								350						
65	TGT	CAG	TAT	GCG	TTT	GAC	TTA	AAA	TGT	GAT	AGT	GTC	TGT	GTC	AAT	GCT	1104		
	Cys	Gln	Tyr	Ala	Phe	Arg	Ile	Leu	Val	Leu	Val	Leu	Val	Leu	Val	Leu			
					355								365						
70	TGT	CAG	TAT	GCG	TTT	GAC	TTA	AAA	TGT	GAT	AGT	GTC	TGT	GTC	AAT	GCT	1152		
	Cys	Gln	Tyr	Ala	Phe	Arg	Ile	Leu	Val	Leu	Val	Leu	Val	Leu	Val	Leu			
					360								370						

106

	370	375	380	
5	TAT CAC TAC GAA CGA GTT GTA TCA CCT GGA ATT GAT CTC TCA GGA TTA Tyr His Tyr Glu Arg Val Val Ser Pro Gly Ile Asp Leu Ser Gly Leu 385 390 395 400	1200		
10	ACA CTG CAG AGT AAT GCT CCA TCA AGT ATG ATG GTG AAG GAT GAA TAT Thr Leu Gln Ser Asn Ala Pro Ser Ser Met Met Val Lys Asp Glu Tyr 405 410 415	1248		
15	GTG CAT GAC TTT GAG GGA CAG CCA TCG TTG TCC ACT GAA GGA CAT TCA Val His Asp Phe Glu Gly Gln Pro Ser Leu Ser Thr Glu Gly His Ser 420 425 430	1296		
20	ATT CAA ACC ATC CAG CAT CCA CCA AGT AAT CGT GCA TCG ACA GAG ACA Ile Gln Thr Ile Gln His Pro Pro Ser Asn Arg Ala Ser Thr Glu Thr 435 440 445	1344		
25	TAC AGC ACC CCA GCT CTG TTA GCC CCA TCT GAG TCT AAT GCT ACC AGC Tyr Ser Thr Pro Ala Leu Leu Ala Pro Ser Glu Ser Asn Ala Thr Ser 450 455 460	1392		
30	ACT GCC AAC TTT CCC AAC ATT CCT GTG GCT TCC ACA AGT CAG CCT GCC Thr Ala Asn Phe Pro Asn Ile Pro Val Ala Ser Thr Ser Gln Pro Ala 465 470 475 480	1440		
35	AGT ATA CTG GGG GGC AGC CAT AGT GAA GGA CTG TTG CAG ATA GCA TCA Ser Ile Leu Gly Gly Ser His Ser Glu Gly Leu Leu Gln Ile Ala Ser 485 490 495	1488		
40	GGG CCT CAG CCA GGA CAG CAG CAG AAT GGA TTT ACT GGT CAG CCA GCT Gly Pro Gln Pro Gly Gln Gln Gln Asn Gly Phe Thr Gly Gln Pro Ala 500 505 510	1536		
45	ACT TAC CAT CAT AAC AGC ACT ACC ACC TGG ACT GGA AGT AGG ACT GCA Thr Tyr His His Asn Ser Thr Thr Thr Trp Thr Gly Ser Arg Thr Ala 515 520 525	1584		
50	CCA TAC ACA CCT AAT TTG CCT CAC CAC CAA AAC GGC CAT CTT CAG CAC Pro Tyr Thr Pro Asn Leu Pro His His Gln Asn Gly His Leu Gln His 530 535 540	1632		
55	CAC CCG CCT ATG CCG CCC CAT CCC GGA CAT TAC TGG CCT GTT CAC AAT His Pro Pro Met Pro Pro His Pro Gly His Tyr Trp Pro Val His Asn 545 550 555 560	1680		
60	GAG CTT GCA TTC CAG CCT CCC ATT TCC AAT CAT CCT GCT CCT GAG TAT Glu Leu Ala Phe Gln Pro Pro Ile Ser Ser Thr Thr Thr Thr Thr Thr Thr Thr 565 570 575 580 585 590	1728		
65	TTT AAG GTT CCT TCA AGC TGC CCT ATT GTT ACT GTT GAT GGA TAC GTT Phe Lys Val Pro Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser 595 600 605 610 615 620 625 630 635 640 645 650	1776		

107

	595	600	605	
5	GAC CCT TCT GGA GGA GAT CGC TTT TGT TTG GGT CAA CTC TCC AAT GTC Asp Pro Ser Gly Gly Asp Arg Phe Cys Leu Gly Gln Leu Ser Asn Val 610 615 620	1872		
10	CAC AGG ACA GAA GCC ATT GAG AGA GCA AGG TTG CAC ATA GGC AAA GGT His Arg Thr Glu Ala Ile Glu Arg Ala Arg Leu His Ile Gly Lys Gly 625 630 635 640	1920		
15	GTG CAG TTG GAA TGT AAA GGT GAA GGT GAT GTT TGG GTC AGG TGC CTT Val Gln Leu Glu Cys Lys Gly Glu Gly Asp Val Trp Val Arg Cys Leu 645 650 655	1968		
20	AGT GAC CAC GCG GTC TTT GTA CAG AGT TAC TAC TTA GAC AGA GAA GCT Ser Asp His Ala Val Phe Val Gln Ser Tyr Tyr Leu Asp Arg Glu Ala 660 665 670	2016		
25	GGG CGT GCA CCT GGA GAT GCT GTT CAT AAG ATC TAC CCA AGT GCA TAT Gly Arg Ala Pro Gly Asp Ala Val His Lys Ile Tyr Pro Ser Ala Tyr 675 680 685	2064		
30	ATA AAG GTC TTT GAT TTG CGT CAG TGT CAT CGA CAG ATG CAG CAG CAG Ile Lys Val Phe Asp Leu Arg Gln Cys His Arg Gln Met Gln Gln Gln 690 695 700	2112		
35	GCG GCT ACT GCA CAA GCT GCA GCA GCT GCC CAG GCA GCA GCC GTG GCA Ala Ala Thr Ala Gln Ala Ala Ala Ala Gln Ala Ala Ala Val Ala 705 710 715 720	2160		
40	GGA AAC ATC CCT GGC CCA GGA TCA GTA GGT GGA ATA GCT CCA GCT ATC Gly Asn Ile Pro Gly Pro Gly Ser Val Gly Gly Ile Ala Pro Ala Ile 725 730 735	2208		
45	AGT CTG TCA GCT GCT GCT GGA ATT GGT GTT GAT GAC CTT CGT CGC TTA Ser Leu Ser Ala Ala Ala Gly Ile Gly Val Asp Asp Leu Arg Arg Leu 740 745 750	2256		
50	TGC ATA CTC AGG ATG AGT TTT GTG AAA GGC TGG GGA CCG GAT TAC CCA Cys Ile Leu Arg Met Ser Phe Val Lys Gly Trp Gly Pro Asp Tyr Pro 755 760 765	2304		
55	AGA CAG AGC ATC AAA GAA ACA CCT TGC TGG ATT GAA ATT CAC TTA CAC Arg Gln Ser Ile Lys Glu Thr Pro Cys Trp Ile Glu Ile His Leu His 770 775 780	2352		
	CGG GCC CTC CAG CTC CTA GAC GAA GTA CTT CAT ACC ATG CCG ATT GCA Arg Ala Leu Gln Leu Leu Asp Gly Gln Val Val Val Val Val Val Val 805	2400		

	Trp	Arg	Trp	Pro	Asp	Leu	His	Lys	Asn	Glu	Leu	Lys	His	Val	Lys	Tyr
			355					360					365			
	Cys	Gln	Tyr	Ala	Phe	Asp	Leu	Lys	Cys	Asp	Ser	Val	Cys	Val	Asn	Pro
		370					375					380				
5	Tyr	His	Tyr	Glu	Arg	Val	Val	Ser	Pro	Gly	Ile	Asp	Leu	Ser	Gly	Leu
	385					390					395					400
	Thr	Leu	Gln	Ser	Asn	Ala	Pro	Ser	Ser	Met	Met	Val	Lys	Asp	Glu	Tyr
					405					410					415	
10	Val	His	Asp	Phe	Glu	Gly	Gln	Pro	Ser	Leu	Ser	Thr	Glu	Gly	His	Ser
				420					425					430		
	Ile	Gln	Thr	Ile	Gln	His	Pro	Pro	Ser	Asn	Arg	Ala	Ser	Thr	Glu	Thr
			435				440						445			
	Tyr	Ser	Thr	Pro	Ala	Leu	Leu	Ala	Pro	Ser	Glu	Ser	Asn	Ala	Thr	Ser
	450						455					460				
15	Thr	Ala	Asn	Phe	Pro	Asn	Ile	Pro	Val	Ala	Ser	Thr	Ser	Gln	Pro	Ala
	465					470					475					480
	Ser	Ile	Leu	Gly	Gly	Ser	His	Ser	Glu	Gly	Leu	Leu	Gln	Ile	Ala	Ser
					485					490					495	
20	Gly	Pro	Gln	Pro	Gly	Gln	Gln	Gln	Asn	Gly	Phe	Thr	Gly	Gln	Pro	Ala
				500					505					510		
	Thr	Tyr	His	His	Asn	Ser	Thr	Thr	Thr	Trp	Thr	Gly	Ser	Arg	Thr	Ala
			515				520						525			
	Pro	Tyr	Thr	Pro	Asn	Leu	Pro	His	His	Gln	Asn	Gly	His	Leu	Gln	His
	530						535					540				
25	His	Pro	Pro	Met	Pro	Pro	His	Pro	Gly	His	Tyr	Trp	Pro	Val	His	Asn
	545					550					555					560
	Glu	Leu	Ala	Phe	Gln	Pro	Pro	Ile	Ser	Asn	His	Pro	Ala	Pro	Glu	Tyr
					565					570					575	
30	Trp	Cys	Ser	Ile	Ala	Tyr	Phe	Glu	Met	Asp	Val	Gln	Val	Gly	Glu	Thr
				580					585					590		
	Phe	Lys	Val	Pro	Ser	Ser	Cys	Pro	Ile	Val	Thr	Val	Asp	Gly	Tyr	Val
			595				600						605			
	Asp	Pro	Ser	Gly	Gly	Asp	Arg	Phe	Cys	Leu	Gly	Gln	Leu	Ser	Asn	Val
	610						615					620				
35	His	Arg	Thr	Glu	Ala	Ile	Glu	Arg	Ala	Arg	Leu	His	Ile	Gly	Lys	Gly
	625					630					635					640
	Val	Gln	Leu	Glu	Cys	Lys	Gly	Glu	Gly	Asp	Val	Trp	Val	Arg	Cys	Leu
					645					650					655	
40	Ser	Asp	His	Ala	Val	Phe	Val	Gln	Ser	Tyr	Tyr	Leu	Asp	Arg	Glu	Ala
				660					665					670		
	Gly	Arg	Ala	Pro	Gly	Asp	Ala	Val	His	Lys	Ile	Tyr	Pro	Ser	Ala	Tyr
			675	</												

110

Asp Pro Gln Pro Leu Asp
805

(2) INFORMATION FOR SEQ ID NO:54:

5

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 3120 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

10

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

15

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...3117

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

20

ATG	GTG	AGC	AAG	GGC	GAG	GAG	CTG	TTC	ACC	GGG	GTG	GTG	CCC	ATC	CTG	48
Met	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	
1				5				10					15			

25

GTC	GAG	CTG	GAC	GGC	GAC	GTA	AAC	GGC	CAC	AAG	TTC	AGC	GTG	TCC	GGC	96
Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	
			20					25					30			

30

GAG	GGC	GAG	GGC	GAT	GCC	ACC	TAC	GGC	AAG	CTG	ACC	CTG	AAG	TTC	ATC	144
Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	
		35					40					45				

35

TGC	ACC	ACC	GGC	AAG	CTG	CCC	GTG	CCC	TGG	CCC	ACC	CTC	GTG	ACC	ACC	192
Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	
		50					55				60					

40

CTG	ACC	TAC	GGC	GTG	CAG	TGC	TTC	AGC	CGC	TAC	CCC	GAC	CAC	ATG	AAG	240
Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	
		65			70				75				80			

45

CAG	CAC	GAC	TTC	TTC	AAG	TCC	GCC	ATG	CCC	GAA	GGC	TAC	GTC	CAG	GAG	288
Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	
			85					90					95			

50

CGC	ACC	ATC	TTC	TTC	AAG	GAC	GAC	GGC	AAC	TAC	AAG	ACC	CGC	GCC	GAG	336
Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	
			100					105					110			

GTG AAG TTC GAG GGC GAG

55

GTG	AAG	TTC	GAG	GGC	GAG	ATC	CTG	GGG	CAC	AAG	CTG	GAG	TAC			432
Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	
		130					135					140				

111

	AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC	480
	Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn	
	145 150 155 160	
5	GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC	528
	Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser	
	165 170 175	
10	GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC	576
	Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly	
	180 185 190	
15	CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG	624
	Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu	
	195 200 205	
20	AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC	672
	Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe	
	210 215 220	
25	GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC	720
	Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser	
	225 230 235 240	
30	GGA CTC AGA TCT ACC ATG GCG GGC TGG ATC CAG GCC CAG CAG CTG CAG	768
	Gly Leu Arg Ser Thr Met Ala Gly Trp Ile Gln Ala Gln Gln Leu Gln	
	245 250 255	
35	GGA GAC GCG CTG CGC CAG ATG CAG GTG CTG TAC GGC CAG CAC TTC CCC	816
	Gly Asp Ala Leu Arg Gln Met Gln Val Leu Tyr Gly Gln His Phe Pro	
	260 265 270	
40	ATC GAG GTC CGG CAC TAC TTG GCC CAG TGG ATT GAG AGC CAG CCA TGG	864
	Ile Glu Val Arg His Tyr Leu Ala Gln Trp Ile Glu Ser Gln Pro Trp	
	275 280 285	
45	GAT GCC ATT GAC TTG GAC AAT CCC CAG GAC AGA GCC CAA GCC ACC CAG	912
	Asp Ala Ile Asp Leu Asp Asn Pro Gln Asp Arg Ala Gln Ala Thr Gln	
	290 295 300	
50	CTC CTG GAG GGC CTG GTG CAG GAG CTG CAG AAG AAG GCG GAG CAC CAG	960
	Leu Leu Glu Gly Leu Val Gln Glu Leu Gln Lys Lys Ala Glu His Gln	
	305 310 315 320	
55	GTG GGG GAA GAT GGG TTT TTA CTG AAG ATC AAG CTG GGG CAC TAC GCC	1008
	Val Gly Glu Asp Gly Phe Leu Leu Lys Ile Lys Leu Gly His Tyr Ala	
	325 330 335	
	ACG CAG CTC CAG AAG AAG	
60	CTC CTG GAG GGC CTG GTG CAG GAG CTG CAG AAG AAG GCG GAG CAC CAG	1104
	Leu Leu Glu Gly Leu Val Gln Glu Leu Gln Lys Lys Ala Glu His Gln	
	340 345 350 355 360 365	
65	Cys Ile Arg His Ile Leu Tyr Asn Glu Gln Arg Leu Val Arg Glu Ala	
	355 360 365	

112

	AAC AAT TGC AGC TCT CCG GCT GGG ATC CTG GTT GAC GCC ATG TCC CAG	1152
	Asn Asn Cys Ser Ser Pro Ala Gly Ile Leu Val Asp Ala Met Ser Gln	
	370 375 380	
5	AAG CAC CTT CAG ATC AAC CAG ACA TTT GAG GAG CTG CGA CTG GTC ACG	1200
	Lys His Leu Gln Ile Asn Gln Thr Phe Glu Glu Leu Arg Leu Val Thr	
	385 390 395 400	
10	CAG GAC ACA GAG AAT GAG CTG AAG AAA CTG CAG CAG ACT CAG GAG TAC	1248
	Gln Asp Thr Glu Asn Glu Leu Lys Lys Leu Gln Gln Thr Gln Glu Tyr	
	405 410 415	
15	TTC ATC ATC CAG TAC CAG GAG AGC CTG AGG ATC CAA GCT CAG TTT GCC	1296
	Phe Ile Ile Gln Tyr Gln Glu Ser Leu Arg Ile Gln Ala Gln Phe Ala	
	420 425 430	
	CAG CTG GCC CAG CTG AGC CCC CAG GAG CGT CTG AGC CGG GAG ACG GCC	1344
	Gln Leu Ala Gln Leu Ser Pro Gln Glu Arg Leu Ser Arg Glu Thr Ala	
	435 440 445	
20	CTC CAG CAG AAG CAG GTG TCT CTG GAG GCC TGG TTG CAG CGT GAG GCA	1392
	Leu Gln Gln Lys Gln Val Ser Leu Glu Ala Trp Leu Gln Arg Glu Ala	
	450 455 460	
25	CAG ACA CTG CAG CAG TAC CGC GTG GAG CTG GCC GAG AAG CAC CAG AAG	1440
	Gln Thr Leu Gln Gln Tyr Arg Val Glu Leu Ala Glu Lys His Gln Lys	
	465 470 475 480	
30	ACC CTG CAG CTG CTG CGG AAG CAG CAG ACC ATC ATC CTG GAT GAC GAG	1488
	Thr Leu Gln Leu Leu Arg Lys Gln Gln Thr Ile Ile Leu Asp Asp Glu	
	485 490 495	
35	CTG ATC CAG TGG AAG CGG CGG CAG CAG CTG GCC GGG AAC GGC GGC CCC	1536
	Leu Ile Gln Trp Lys Arg Arg Gln Gln Leu Ala Gly Asn Gly Gly Pro	
	500 505 510	
	CCC GAG GGC AGC CTG GAC GTG CTA CAG TCC TGG TGT GAG AAG TTG GCC	1584
	Pro Glu Gly Ser Leu Asp Val Leu Gln Ser Trp Cys Glu Lys Leu Ala	
	515 520 525	
40	GAG ATC ATC TGG CAG AAC CGG CAG CAG ATC CGC AGG GCT GAG CAC CTC	1632
	Glu Ile Ile Trp Gln Asn Arg Gln Gln Ile Arg Arg Ala Glu His Leu	
	530 535 540	
45	TGC CAG CAG CTG CCC ATC CCC GGC CCA GTG GAG GAG ATG CTG GCC GAG	1680
	Cys Gln Gln Leu Pro Ile Pro Gly Pro Val Glu Glu Met Leu Ala Glu	
	545 550 555 560	
	GTC AAC GCC ACC ATC ACC GGC GGC GGC GGC GGC GGC GGC GGC GGC	
	565 570 575 580 585 590 595 600 605 610 615 620 625 630	
55	Phe Ile Ile Glu Lys Gln Pro Pro Gln Val Leu Lys Thr Gln Thr Lys	1776
	580 585 590	

	TTT	GCA	GCC	ACC	GTA	CGC	CTG	CTG	GTG	GGC	GGG	AAG	CTG	AAC	GTG	CAC	1824
	Phe	Ala	Ala	Thr	Val	Arg	Leu	Leu	Val	Gly	Gly	Lys	Leu	Asn	Val	His	
			595					600					605				
5	ATG	AAT	CCC	CCC	CAG	GTG	AAG	GCC	ACC	ATC	ATC	AGT	GAG	CAG	CAG	GCC	1872
	Met	Asn	Pro	Pro	Gln	Val	Lys	Ala	Thr	Ile	Ile	Ser	Glu	Gln	Gln	Ala	
			610				615					620					
10	AAG	TCT	CTG	CTT	AAA	AAT	GAG	AAC	ACC	CGC	AAC	GAG	TGC	AGT	GGT	GAG	1920
	Lys	Ser	Leu	Leu	Lys	Asn	Glu	Asn	Thr	Arg	Asn	Glu	Cys	Ser	Gly	Glu	
			625			630					635					640	
15	ATC	CTG	AAC	AAC	TGC	TGC	GTG	ATG	GAG	TAC	CAC	CAA	GCC	ACG	GGC	ACC	1968
	Ile	Leu	Asn	Asn	Cys	Cys	Val	Met	Glu	Tyr	His	Gln	Ala	Thr	Gly	Thr	
					645					650					655		
20	CTC	AGT	GCC	CAC	TTC	AGG	AAC	ATG	TCA	CTG	AAG	AGG	ATC	AAG	CGT	GCT	2016
	Leu	Ser	Ala	His	Phe	Arg	Asn	Met	Ser	Leu	Lys	Arg	Ile	Lys	Arg	Ala	
				660					665					670			
25	GAC	CGG	CGG	GGT	GCA	GAG	TCC	GTG	ACA	GAG	GAG	AAG	TTC	ACA	GTC	CTG	2064
	Asp	Arg	Arg	Gly	Ala	Glu	Ser	Val	Thr	Glu	Glu	Lys	Phe	Thr	Val	Leu	
				675				680					685				
30	TTT	GAG	TCT	CAG	TTC	AGT	GTT	GGC	AGC	AAT	GAG	CTT	GTG	TTC	CAG	GTG	2112
	Phe	Glu	Ser	Gln	Phe	Ser	Val	Gly	Ser	Asn	Glu	Leu	Val	Phe	Gln	Val	
			690				695					700					
35	AAG	ACT	CTG	TCC	CTA	CCT	GTG	GTT	GTC	ATC	GTC	CAC	GGC	AGC	CAG	GAC	2160
	Lys	Thr	Leu	Ser	Leu	Pro	Val	Val	Val	Ile	Val	His	Gly	Ser	Gln	Asp	
			705			710					715					720	
40	CAC	AAT	GCC	ACG	GCT	ACT	GTG	CTG	TGG	GAC	AAT	GCC	TTT	GCT	GAG	CCG	2208
	His	Asn	Ala	Thr	Ala	Thr	Val	Leu	Trp	Asp	Asn	Ala	Phe	Ala	Glu	Pro	
				725						730				735			
45	GGC	AGG	GTG	CCA	TTT	GCC	GTG	CCT	GAC	AAA	GTG	CTG	TGG	CCG	CAG	CTG	2256
	Gly	Arg	Val	Pro	Phe	Ala	Val	Pro	Asp	Lys	Val	Leu	Trp	Pro	Gln	Leu	
				740					745					750			
50	TGT	GAG	GCG	CTC	AAC	ATG	AAA	TTC	AAG	GCC	GAA	GTG	CAG	AGC	AAC	CGG	2304
	Cys	Glu	Ala	Leu	Asn	Met	Lys	Phe	Lys	Ala	Glu	Val	Gln	Ser	Asn	Arg	
				755			760						765				
55	GGC	CTG	ACC	AAG	GAG	AAC	CTC	GTG	TTC	CTG	GCG	CAG	AAA	CTG	TTC	AAC	2352
	Gly	Leu	Thr	Lys	Glu	Asn	Leu	Val	Phe	Leu	Ala	Gln	Lys	Leu	Phe	Asn	
			770				775					780					
-	AAC	AGC	AGC	AGC	GAG	CTG	GAG	CTG	ATT	GGA	AGA	ATA	ATA	ATA	ATA	ATA	
55	Ser	Gln	Phe	Asn	Arg	Glu	Asn	Leu</									

114

	CAG TGG TTT GAC GGG GTG ATG GAG GTG TTG AAG AAG CAC CAC AAG CCC	2496
	Gln Trp Phe Asp Gly Val Met Glu Val Leu Lys Lys His His Lys Pro	
	820 825 830	
5	CAC TGG AAT GAT GGG GCC ATC CTA GGT TTT GTG AAT AAG CAA CAG GCC	2544
	His Trp Asn Asp Gly Ala Ile Leu Gly Phe Val Asn Lys Gln Gln Ala	
	835 840 845	
10	CAC GAC CTG CTC ATC AAC AAG CCC GAC GGG ACC TTC TTG TTG CGC TTT	2592
	His Asp Leu Leu Ile Asn Lys Pro Asp Gly Thr Phe Leu Leu Arg Phe	
	850 855 860	
15	AGT GAC TCA GAA ATC GGG GGC ATC ACC ATC GCC TGG AAG TTT GAC TCC	2640
	Ser Asp Ser Glu Ile Gly Gly Ile Thr Ile Ala Trp Lys Phe Asp Ser	
	865 870 875 880	
20	CCG GAA CGC AAC CTG TGG AAC CTG AAA CCA TTC ACC ACG CGG GAT TTC	2688
	Pro Glu Arg Asn Leu Trp Asn Leu Lys Pro Phe Thr Thr Arg Asp Phe	
	885 890 895	
25	TCC ATC AGG TCC CTG GCT GAC CGG CTG GGG GAC CTG AGC TAT CTC ATC	2736
	Ser Ile Arg Ser Leu Ala Asp Arg Leu Gly Asp Leu Ser Tyr Leu Ile	
	900 905 910	
30	TAT GTG TTT CCT GAC CGC CCC AAG GAT GAG GTC TTC TCC AAG TAC TAC	2784
	Tyr Val Phe Pro Asp Arg Pro Lys Asp Glu Val Phe Ser Lys Tyr Tyr	
	915 920 925	
35	ACT CCT GTG CTG GCT AAA GCT GTT GAT GGA TAT GTG AAA CCA CAG ATC	2832
	Thr Pro Val Leu Ala Lys Ala Val Asp Gly Tyr Val Lys Pro Gln Ile	
	930 935 940	
40	AAG CAA GTG GTC CCT GAG TTT GTG AAT GCA TCT GCA GAT GCT GGG GGC	2880
	Lys Gln Val Val Pro Glu Phe Val Asn Ala Ser Ala Asp Ala Gly Gly	
	945 950 955 960	
45	AGC AGC GCC ACG TAC ATG GAC CAG GCC CCC TCC CCA GCT GTG TGC CCC	2928
	Ser Ser Ala Thr Tyr Met Asp Gln Ala Pro Ser Pro Ala Val Cys Pro	
	965 970 975	
50	CAG GCT CCC TAT AAC ATG TAC CCA CAG AAC CCT GAC CAT GTA CTC GAT	2976
	Gln Ala Pro Tyr Asn Met Tyr Pro Gln Asn Pro Asp His Val Leu Asp	
	980 985 990	
55	CAG GAT GGA GAA TTC GAC CTG GAT GAG ACC ATG GAT GTG GCC AGG CAC	3024
	Gln Asp Gly Glu Phe Asp Leu Asp Glu Thr Met Asp Val Ala Arg His	
	995 1000 1005	
60	GTG GAG GAA CTC TTA GGG GAA GAT GAG GTC GGC TCC CTC TCA TGA	3120
	Ser Pro Pro Ala Gly Leu Phe Thr Ser Ala Arg Gly Ser Leu Ser	
	1025 1030 1035 1	

115

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 1039 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

- 10 (ii) MOLECULE TYPE: protein
 (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

```

15 Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
    1           5           10           15
    Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
        20           25           30
    Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
20      35           40           45
    Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50           55           60
    Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
    65           70           75           80
25 Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
    85           90           95
    Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
    100          105          110
    Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
30      115          120          125
    Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130          135          140
    Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
    145          150          155          160
35 Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
    165          170          175
    Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
    180          185          190
    Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
40      195          200          205
    Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210          215          220
    Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
    225          230          235          240
45 Gly Leu Arg Ser Thr Met Ala Gly Trp Ile Gln Ala Gln Gln Leu Gln
    245          250          255
    Gly Asp Ala Leu Arg Gln Met Gln Val Leu Tyr Gly Gln His Phe Pro
    260          265          270
    Ile Glu Val Arg His Thr ...

...
    ... Lys Lys Ala Glu His Gln
    305          310          315          320
55 Val Gly Glu Asp Gly Phe Leu Leu Lys Ile Lys Leu Gly His Tyr Ala
    325          330

```

	Thr	Gln	Leu	Gln	Lys	Thr	Tyr	Asp	Arg	Cys	Pro	Leu	Glu	Leu	Val	Arg
				340					345					350		
	Cys	Ile	Arg	His	Ile	Leu	Tyr	Asn	Glu	Gln	Arg	Leu	Val	Arg	Glu	Ala
			355					360					365			
5	Asn	Asn	Cys	Ser	Ser	Pro	Ala	Gly	Ile	Leu	Val	Asp	Ala	Met	Ser	Gln
			370				375					380				
	Lys	His	Leu	Gln	Ile	Asn	Gln	Thr	Phe	Glu	Glu	Leu	Arg	Leu	Val	Thr
	385					390					395					400
10	Gln	Asp	Thr	Glu	Asn	Glu	Leu	Lys	Lys	Leu	Gln	Gln	Thr	Gln	Glu	Tyr
				405						410					415	
	Phe	Ile	Ile	Gln	Tyr	Gln	Glu	Ser	Leu	Arg	Ile	Gln	Ala	Gln	Phe	Ala
				420					425					430		
	Gln	Leu	Ala	Gln	Leu	Ser	Pro	Gln	Glu	Arg	Leu	Ser	Arg	Glu	Thr	Ala
			435					440					445			
15	Leu	Gln	Gln	Lys	Gln	Val	Ser	Leu	Glu	Ala	Trp	Leu	Gln	Arg	Glu	Ala
		450					455					460				
	Gln	Thr	Leu	Gln	Gln	Tyr	Arg	Val	Glu	Leu	Ala	Glu	Lys	His	Gln	Lys
	465					470					475					480
20	Thr	Leu	Gln	Leu	Leu	Arg	Lys	Gln	Gln	Thr	Ile	Ile	Leu	Asp	Asp	Glu
				485						490					495	
	Leu	Ile	Gln	Trp	Lys	Arg	Arg	Gln	Gln	Leu	Ala	Gly	Asn	Gly	Gly	Pro
			500						505					510		
	Pro	Glu	Gly	Ser	Leu	Asp	Val	Leu	Gln	Ser	Trp	Cys	Glu	Lys	Leu	Ala
		515						520					525			
25	Glu	Ile	Ile	Trp	Gln	Asn	Arg	Gln	Gln	Ile	Arg	Arg	Ala	Glu	His	Leu
		530					535					540				
	Cys	Gln	Gln	Leu	Pro	Ile	Pro	Gly	Pro	Val	Glu	Glu	Met	Leu	Ala	Glu
	545					550					555					560
30	Val	Asn	Ala	Thr	Ile	Thr	Asp	Ile	Ile	Ser	Ala	Leu	Val	Thr	Ser	Thr
				565						570					575	
	Phe	Ile	Ile	Glu	Lys	Gln	Pro	Pro	Gln	Val	Leu	Lys	Thr	Gln	Thr	Lys
			580						585					590		
	Phe	Ala	Ala	Thr	Val	Arg	Leu	Leu	Val	Gly	Gly	Lys	Leu	Asn	Val	His
		595						600					605			
35	Met	Asn	Pro	Pro	Gln	Val	Lys	Ala	Thr	Ile	Ile	Ser	Glu	Gln	Gln	Ala
		610					615						620			
	Lys	Ser	Leu	Leu	Lys	Asn	Glu	Asn	Thr	Arg	Asn	Glu	Cys	Ser	Gly	Glu
	625					630					635					640
40	Ile	Leu	Asn	Asn	Cys	Cys	Val	Met	Glu	Tyr	His	Gln	Ala	Thr	Gly	Thr
				645						650					655	
	Leu	Ser	Ala	His	Phe	Arg	Asn	Met	Ser	Leu	Lys	Arg	Ile	Lys	Arg	Ala

117

Asn Ser Ser Ser His Leu Glu Asp Tyr Ser Gly Leu Ser Val Ser Trp
 785 790 795 800
 Ser Gln Phe Asn Arg Glu Asn Leu Pro Gly Trp Asn Tyr Thr Phe Trp
 805 810 815
 5 Gln Trp Phe Asp Gly Val Met Glu Val Leu Lys Lys His His Lys Pro
 820 825 830
 His Trp Asn Asp Gly Ala Ile Leu Gly Phe Val Asn Lys Gln Gln Ala
 835 840 845
 10 His Asp Leu Leu Ile Asn Lys Pro Asp Gly Thr Phe Leu Leu Arg Phe
 850 855 860
 Ser Asp Ser Glu Ile Gly Gly Ile Thr Ile Ala Trp Lys Phe Asp Ser
 865 870 875 880
 Pro Glu Arg Asn Leu Trp Asn Leu Lys Pro Phe Thr Thr Arg Asp Phe
 885 890 895
 15 Ser Ile Arg Ser Leu Ala Asp Arg Leu Gly Asp Leu Ser Tyr Leu Ile
 900 905 910
 Tyr Val Phe Pro Asp Arg Pro Lys Asp Glu Val Phe Ser Lys Tyr Tyr
 915 920 925
 20 Thr Pro Val Leu Ala Lys Ala Val Asp Gly Tyr Val Lys Pro Gln Ile
 930 935 940
 Lys Gln Val Val Pro Glu Phe Val Asn Ala Ser Ala Asp Ala Gly Gly
 945 950 955 960
 Ser Ser Ala Thr Tyr Met Asp Gln Ala Pro Ser Pro Ala Val Cys Pro
 965 970 975
 25 Gln Ala Pro Tyr Asn Met Tyr Pro Gln Asn Pro Asp His Val Leu Asp
 980 985 990
 Gln Asp Gly Glu Phe Asp Leu Asp Glu Thr Met Asp Val Ala Arg His
 995 1000 1005
 Val Glu Glu Leu Leu Arg Arg Pro Met Asp Ser Leu Asp Ser Arg Leu
 1010 1015 1020
 30 Ser Pro Pro Ala Gly Leu Phe Thr Ser Ala Arg Gly Ser Leu Ser
 025 1030 1035 1

(2) INFORMATION FOR SEQ ID NO:56:

35

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1875 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

45

- (A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...1872
 (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:

50

15

55

GGA ACT GCT GGG GTC GTC CCG GTG GTC CCC GGG GAG GTG GAG GTG GTG
 Gly Thr Ala Gly Val Val Pro Val Val Pro Gly Glu Val Glu Val Val

96

	118																	
	20						25						30					
5	AAG	GGG	CAG	CCA	TTC	GAT	GTG	GGC	CCA	CGC	TAC	ACG	CAG	CTG	CAG	TAC		144
	Lys	Gly	Gln	Pro	Phe	Asp	Val	Gly	Pro	Arg	Tyr	Thr	Gln	Leu	Gln	Tyr		
	35						40						45					
10	ATC	GGC	GAG	GGC	GCG	TAC	GGC	ATG	GTC	AGC	TCA	GCT	TAT	GAC	CAC	GTG		192
	Ile	Gly	Glu	Gly	Ala	Tyr	Gly	Met	Val	Ser	Ser	Ala	Tyr	Asp	His	Val		
	50						55						60					
15	CGC	AAG	ACC	AGA	GTG	GCC	ATC	AAG	AAG	ATC	AGC	CCC	TTT	GAG	CAT	CAA		240
	Arg	Lys	Thr	Arg	Val	Ala	Ile	Lys	Lys	Ile	Ser	Pro	Phe	Glu	His	Gln		
	65						70						75					
20	ACC	TAC	TGT	CAG	CGC	ACG	CTG	AGG	GAG	ATC	CAG	ATC	TTG	CTG	CGA	TTC		288
	Thr	Tyr	Cys	Gln	Arg	Thr	Leu	Arg	Glu	Ile	Gln	Ile	Leu	Leu	Arg	Phe		
	85						90						95					
25	CGC	CAT	GAG	AAT	GTT	ATA	GGC	ATC	CGA	GAC	ATC	CTC	AGA	GCG	CCC	ACC		336
	Arg	His	Glu	Asn	Val	Ile	Gly	Ile	Arg	Asp	Ile	Leu	Arg	Ala	Pro	Thr		
	100						105						110					
30	CTG	GAA	GCC	ATG	AGA	GAT	GTT	TAC	ATT	GTT	CAG	GAC	CTC	ATG	GAG	ACA		384
	Leu	Glu	Ala	Met	Arg	Asp	Val	Tyr	Ile	Val	Gln	Asp	Leu	Met	Glu	Thr		
	115						120						125					
35	GAC	CTG	TAC	AAG	CTG	CTT	AAA	AGC	CAG	CAG	CTG	AGC	AAT	GAC	CAC	ATC		432
	Asp	Leu	Tyr	Lys	Leu	Leu	Lys	Ser	Gln	Gln	Leu	Ser	Asn	Asp	His	Ile		
	130						135						140					
40	TGC	TAC	TTC	CTC	TAC	CAG	ATC	CTC	CGG	GGC	CTC	AAG	TAT	ATA	CAC	TCA		480
	Cys	Tyr	Phe	Leu	Tyr	Gln	Ile	Leu	Arg	Gly	Leu	Lys	Tyr	Ile	His	Ser		
	145						150						155					
45	GCC	AAT	GTG	CTG	CAC	CGG	GAC	CTG	AAG	CCT	TCC	AAT	CTG	CTT	ATC	AAC		528
	Ala	Asn	Val	Leu	His	Arg	Asp	Leu	Lys	Pro	Ser	Asn	Leu	Leu	Ile	Asn		
	165						170						175					
50	ACC	ACC	TGC	GAC	CTT	AAG	ATC	TGT	GAT	TTT	GGC	CTG	GCC	CGG	ATT	GCT		576
	Thr	Thr	Cys	Asp	Leu	Lys	Ile	Cys	Asp	Phe	Gly	Leu	Ala	Arg	Ile	Ala		
	180						185						190					
55	GAC	CCT	GAG	CAC	GAC	CAC	ACT	GGC	TTT	CTG	ACG	GAG	TAT	GTG	GCC	ACA		624
	Asp	Pro	Glu	His	Asp	His	Thr	Gly	Phe	Leu	Thr	Glu	Tyr	Val	Ala	Thr		
	195						200						205					
60	CGC	TGG	TAC	CGA	GCC	CCA	GAG	ATC	ATG	CTT	AAT	TCC	AAG	GGC	TAC	ACC		672
	Arg	Trp	Tyr	Arg	Ala	Pro	Glu	Ile	Met	Leu	Asn	Ser	Lys	Gln	Thr	Thr		
	210						215						220					
65	TCC	AAC	CGG	CCC	ATC	TTC	CCC	GGC	AAG	CAC	TAC	CTG	GAC	CAG	CTC	AAC		768
	Ser	Asn	Arg	Pro	Ile	Phe	Pro	Gly	Lys	His	Tyr	Leu	Arg	Ala	Ala	Ala		
	230						235						240					

SUBSTITUTE SHEET (RULE 26)

(2) INFORMATION FOR SEQ ID NO:57:

(A) LENGTH: 624 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(11) MOLECULE TYPE

Met Ala Ala Ala Ala Ala Ala Pro Gly Gly Gly Gly Gly Glu Pro Arg
55 1 5 10 15
Gly Thr Ala Gly Val Val Pro Val Val Pro Gly Gly Val Val Val Val

				20					25					30			
	Lys	Gly	Gln	Pro	Phe	Asp	Val	Gly	Pro	Arg	Tyr	Thr	Gln	Leu	Gln	Tyr	
			35					40					45				
5	Ile	Gly	Glu	Gly	Ala	Tyr	Gly	Met	Val	Ser	Ser	Ala	Tyr	Asp	His	Val	
		50					55					60					
	Arg	Lys	Thr	Arg	Val	Ala	Ile	Lys	Lys	Ile	Ser	Pro	Phe	Glu	His	Gln	
	65					70					75					80	
	Thr	Tyr	Cys	Gln	Arg	Thr	Leu	Arg	Glu	Ile	Gln	Ile	Leu	Leu	Arg	Phe	
					85					90					95		
10	Arg	His	Glu	Asn	Val	Ile	Gly	Ile	Arg	Asp	Ile	Leu	Arg	Ala	Pro	Thr	
				100					105					110			
	Leu	Glu	Ala	Met	Arg	Asp	Val	Tyr	Ile	Val	Gln	Asp	Leu	Met	Glu	Thr	
			115					120					125				
15	Asp	Leu	Tyr	Lys	Leu	Leu	Lys	Ser	Gln	Gln	Leu	Ser	Asn	Asp	His	Ile	
		130					135					140					
	Cys	Tyr	Phe	Leu	Tyr	Gln	Ile	Leu	Arg	Gly	Leu	Lys	Tyr	Ile	His	Ser	
	145					150					155					160	
	Ala	Asn	Val	Leu	His	Arg	Asp	Leu	Lys	Pro	Ser	Asn	Leu	Leu	Ile	Asn	
					165					170					175		
20	Thr	Thr	Cys	Asp	Leu	Lys	Ile	Cys	Asp	Phe	Gly	Leu	Ala	Arg	Ile	Ala	
				180					185					190			
	Asp	Pro	Glu	His	Asp	His	Thr	Gly	Phe	Leu	Thr	Glu	Tyr	Val	Ala	Thr	
			195					200					205				
25	Arg	Trp	Tyr	Arg	Ala	Pro	Glu	Ile	Met	Leu	Asn	Ser	Lys	Gly	Tyr	Thr	
		210					215					220					
	Lys	Ser	Ile	Asp	Ile	Trp	Ser	Val	Gly	Cys	Ile	Leu	Ala	Glu	Met	Leu	
	225					230					235					240	
	Ser	Asn	Arg	Pro	Ile	Phe	Pro	Gly	Lys	His	Tyr	Leu	Asp	Gln	Leu	Asn	
					245					250					255		
30	His	Ile	Leu	Gly	Ile	Leu	Gly	Ser	Pro	Ser	Gln	Glu	Asp	Leu	Asn	Cys	
				260					265					270			
	Ile	Ile	Asn	Met	Lys	Ala	Arg	Asn	Tyr	Leu	Gln	Ser	Leu	Pro	Ser	Lys	
			275					280					285				
35	Thr	Lys	Val	Ala	Trp	Ala	Lys	Leu	Phe	Pro	Lys	Ser	Asp	Ser	Lys	Ala	
		290					295					300					
	Leu	Asp	Leu	Leu	Asp	Arg	Met	Leu	Thr	Phe	Asn	Pro	Asn	Lys	Arg	Ile	
		305				310					315					320	
	Thr	Val	Glu	Glu	Ala	Leu	Ala	His	Pro	Tyr	Leu	Glu	Gln	Tyr	Tyr	Asp	
				325					330						335		
40	Pro	Thr	Asp	Glu	Pro	Val	Ala	Glu	Glu	Pro	Phe						

122

465 470 475 480
 Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
 485 490 495
 Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
 500 505 510
 5 Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met Glu Tyr Asn Tyr
 515 520 525
 Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro Lys Asn Gly Ile
 530 535 540
 10 Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp Gly Ser Val Gln
 545 550 555 560
 Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
 565 570 575
 Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
 580 585 590
 15 Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu Glu Phe Val Thr
 595 600 605
 Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys Pro Gln Glu
 610 615 620

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1815 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- (A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...1811
 (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

ATG GCG GCG GCG GCG GCG GCG GCG GCG GAG ATG GTC CGC GGG CAG GTG 48
 Met Ala Ala Ala Ala Ala Ala Gly Pro Glu Met Val Arg Gly Gln Val
 40 1 5 10 15
 TTC GAC GTG GGG CCG CGC TAC ACT AAT CTC TCG TAC ATC GGA GAA GGC 96
 Phe Asp Val Gly Pro Arg Tyr Thr Asn Leu Ser Tyr Ile Gly Glu Gly
 20 25 30
 45 GCC TAC GGC ATG GTT TGT TCT GCT TAT GAT AAT CTC AAC AAA GTT CGA 144
 Ala Tyr Gly Met Val Cys Ser Ala Tyr Asp Asn Leu Asn Lys Val Arg
 35 40 45
 AGA ACC CTG AGA GAG ATA AAA ATC CTA CTG CGC TTC AGA CAT GAG AAC 240
 55 Arg Thr Leu Arg Glu Ile Lys Ile Leu Leu Arg Phe Arg His Glu Asn
 65 70 75 80

123

5	ATC ATC GGC ATC AAT GAC ATC ATC CGG GCA CCA ACC ATT GAG CAG ATG	288
	Ile Ile Gly Ile Asn Asp Ile Ile Arg Ala Pro Thr Ile Glu Gln Met	
	85 90 95	
10	AAA GAT GTA TAT ATA GTA CAG GAC CTC ATG GAG ACA GAT CTT TAC AAG	336
	Lys Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys	
	100 105 110	
15	CTC TTG AAG ACA CAG CAC CTC AGC AAT GAT CAT ATC TGC TAT TTT CTT	384
	Leu Leu Lys Thr Gln His Leu Ser Asn Asp His Ile Cys Tyr Phe Leu	
	115 120 125	
20	TAT CAG ATC CTG AGA GGA TTA AAG TAT ATA CAT TCA GCT AAT GTT CTG	432
	Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala Asn Val Leu	
	130 135 140	
25	CAC CGT GAC CTC AAG CCT TCC AAC CTC CTG CTG AAC ACC ACT TGT GAT	480
	His Arg Asp Leu Lys Pro Ser Asn Leu Leu Leu Asn Thr Thr Cys Asp	
	145 150 155 160	
30	CTC AAG ATC TGT GAC TTT GGC CTT GCC CGT GTT GCA GAT CCA GAC CAT	528
	Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Val Ala Asp Pro Asp His	
	165 170 175	
35	GAT CAT ACA GGG TTC TTG ACA GAG TAT GTA GCC ACG CGT TGG TAC AGA	576
	Asp His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg Trp Tyr Arg	
	180 185 190	
40	GCT CCA GAA ATT ATG TTG AAT TCC AAG GGT TAT ACC AAG TCC ATT GAT	624
	Ala Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys Ser Ile Asp	
	195 200 205	
45	ATT TGG TCT GTG GGC TGC ATC CTG GCA GAG ATG CTA TCC AAC AGG CCT	672
	Ile Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser Asn Arg Pro	
	210 215 220	
50	ATC TTC CCA GGA AAG CAT TAC CTT GAC CAG CTG AAT CAC ATC CTG GGT	720
	Ile Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His Ile Leu Gly	
	225 230 235 240	
55	ATT CTT GGA TCT CCA TCA CAG GAA GAT CTG AAT TGT ATA ATA AAT TTA	768
	Ile Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile Ile Asn Leu	
	245 250 255	
60	AAA GCT AGA AAC TAT TTG CTT TCT CTC CCG CAC AAA AAT AAG GTG CCG	816
	Lys Ala Arg Asn Tyr Leu Leu Ser Leu Pro His Lys Asn Lys Val Pro	
	260 265 270	
65	GAT AAA ATG TTG ACA TTT AAC CCT CAC AAG AGG ATT GAA GTT GAA CAG	912
	Asp Lys Met Leu Thr Phe Asn Pro His Lys Arg Ile Glu Val Glu Gln	
	280 285 290	

124

5	GCT CTG GCC CAC CCG TAC CTG GAG CAG TAT TAT GAC CCA AGT GAT GAG	960
	Ala Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro Ser Asp Glu	
	305 310 315 320	
10	CCC ATT GCT GAA GCA CCA TTC AAG TTT GAC ATG GAG CTG GAC GAC TTA	1008
	Pro Ile Ala Glu Ala Pro Phe Lys Phe Asp Met Glu Leu Asp Asp Leu	
	325 330 335	
15	CCT AAG GAG AAG CTC AAA GAA CTC ATT TTT GAA GAG ACT GCT CGA TTC	1056
	Pro Lys Glu Lys Leu Lys Glu Leu Ile Phe Glu Glu Thr Ala Arg Phe	
	340 345 350	
20	CAG CCA GGA TAC AGA TCT ATG GAT CCA CCG GTC GCC ACC ATG GTG AGC	1104
	Gln Pro Gly Tyr Arg Ser Met Asp Pro Pro Val Ala Thr Met Val Ser	
	355 360 365	
25	AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC GAG CTG	1152
	Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu	
	370 375 380	
30	GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG GGC GAG	1200
	Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu	
	385 390 395 400	
35	GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC ACC ACC	1248
	Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr	
	405 410 415	
40	GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG ACC TAC	1296
	Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr	
	420 425 430	
45	GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG CAC GAC	1344
	Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp	
	435 440 445	
50	TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC ACC ATC	1392
	Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile	
	450 455 460	
55	TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG AAG TTC	1440
	Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe	
	465 470 475 480	
60	GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC GAC TTC	1488
	Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe	
	485 490 495	
65	AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG	1584
	Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys	
	515 520 525	

125

5 GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC 1632
 Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu
 530 535 540
 GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG 1680
 Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu
 545 550 555 560
 10 CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC 1728
 Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp
 565 570 575
 15 CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC 1776
 Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala
 580 585 590
 20 GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AA GTAA 1815
 Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
 595 600

(2) INFORMATION FOR SEQ ID NO:59:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 604 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 30 (ii) MOLECULE TYPE: protein
 (v) FRAGMENT TYPE: internal
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:
 35 Met Ala Ala Ala Ala Ala Ala Gly Pro Glu Met Val Arg Gly Gln Val
 1 5 10 15
 Phe Asp Val Gly Pro Arg Tyr Thr Asn Leu Ser Tyr Ile Gly Glu Gly
 20 25 30
 40 Ala Tyr Gly Met Val Cys Ser Ala Tyr Asp Asn Leu Asn Lys Val Arg
 35 40 45
 Val Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr Tyr Cys Gln
 50 55 60
 45 Arg Thr Leu Arg Glu Ile Lys Ile Leu Leu Arg Phe Arg His Glu Asn
 65 70 75 80
 Ile Ile Gly Ile Asn Asp Ile Ile Arg Ala Pro Thr Ile Glu Gln Met
 85 90 95
 Lys Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys
 100
 110 120 130 140
 55 His Arg Asp Leu Lys Pro Ser Asn Leu Leu Leu Asn Thr Thr Cys Asp
 145 150 155 160
 Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Val Ala Asp Phe Lys Phe

SUBSTITUTE SHEET (RULE 26)

127

(2) INFORMATION FOR SEQ ID NO:60:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 2511 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- 15 (A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...2508
 (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

20	ATG GAG CTG GAA AAC ATC GTG GCC AAC ACG GTC TTG CTG AAA GCC AGG Met Glu Leu Glu Asn Ile Val Ala Asn Thr Val Leu Leu Lys Ala Arg 1 5 10 15	48
25	GAA GGG GGC GGA GGA AAG CGC AAA GGG AAA AGC AAG AAG TGG AAA GAA Glu Gly Gly Gly Gly Lys Arg Lys Gly Lys Ser Lys Lys Trp Lys Glu 20 25 30	96
30	ATC CTG AAG TTC CCT CAC ATT AGC CAG TGT GAA GAC CTC CGA AGG ACC Ile Leu Lys Phe Pro His Ile Ser Gln Cys Glu Asp Leu Arg Arg Thr 35 40 45	144
35	ATA GAC AGA GAT TAC TGC AGT TTA TGT GAC AAG CAG CCA ATC GGG AGG Ile Asp Arg Asp Tyr Cys Ser Leu Cys Asp Lys Gln Pro Ile Gly Arg 50 55 60	192
40	CTG CTT TTC CGG CAG TTT TGT GAA ACC AGG CCT GGG CTG GAG TGT TAC Leu Leu Phe Arg Gln Phe Cys Glu Thr Arg Pro Gly Leu Glu Cys Tyr 65 70 75 80	240
45	ATT CAG TTC CTG GAC TCC GTG GCA GAA TAT GAA GTT ACT CCA GAT GAA Ile Gln Phe Leu Asp Ser Val Ala Glu Tyr Glu Val Thr Pro Asp Glu 85 90 95	288
50	AAA CTG GGA GAG AAA GGG AAG GAA ATT ATG ACC AAG TAC CTC ACC CCA Lys Leu Gly Glu Lys Gly Lys Glu Ile Met Thr Lys Tyr Leu Thr Pro 100 105 110	336
55	AAG TCC CCT GTT TTC ATA GCC CAA GTT GGC CAA GAC CTG GTC TCC CAG Lys Ser Pro Val Phe Ile Ala Gln Val Gly Gln Asp Leu Val Ser Gln 115 120 125	384
60	TGT GCA CAG TCT GTC CAC GAG TAC CTG AGG GGA GAA CCA TTC CAC GAA Cys Ala Gln Ser Val His Glu Tyr Leu Arg Gly Glu Pro Phe His Glu 145 150 155 160	480

128

5	TAT CTG GAC AGC ATG TTT TTT GAC CGC TTT CTC CAG TGG AAG TGG TTG	528
	Tyr Leu Asp Ser Met Phe Phe Asp Arg Phe Leu Gln Trp Lys Trp Leu	
	165 170 175	
10	GAA AGG CAA CCG GTG ACC AAA AAC ACT TTC AGG CAG TAT CGA GTG CTA	576
	Glu Arg Gln Pro Val Thr Lys Asn Thr Phe Arg Gln Tyr Arg Val Leu	
	180 185 190	
15	GGA AAA GGG GGC TTC GGG GAG GTC TGT GCC TGC CAG GTT CGG GCC ACG	624
	Gly Lys Gly Gly Phe Gly Glu Val Cys Ala Cys Gln Val Arg Ala Thr	
	195 200 205	
20	GGT AAA ATG TAT GCC TGC AAG CGC TTG GAG AAG AAG AGG ATC AAA AAG	672
	Gly Lys Met Tyr Ala Cys Lys Arg Leu Glu Lys Lys Arg Ile Lys Lys	
	210 215 220	
25	AGG AAA GGG GAG TCC ATG GCC CTC AAT GAG AAG CAG ATC CTC GAG AAG	720
	Arg Lys Gly Glu Ser Met Ala Leu Asn Glu Lys Gln Ile Leu Glu Lys	
	225 230 235 240	
30	GTC AAC AGT CAG TTT GTG GTC AAC CTG GCC TAT GCC TAC GAG ACC AAG	768
	Val Asn Ser Gln Phe Val Val Asn Leu Ala Tyr Ala Tyr Glu Thr Lys	
	245 250 255	
35	GAT GCA CTG TGC TTG GTC CTG ACC ATC ATG AAT GGG GGT GAC CTG AAG	816
	Asp Ala Leu Cys Leu Val Leu Thr Ile Met Asn Gly Gly Asp Leu Lys	
	260 265 270	
40	TTC CAC ATC TAC AAC ATG GGC AAC CCT GGC TTC GAG GAG GAG CGG GCC	864
	Phe His Ile Tyr Asn Met Gly Asn Pro Gly Phe Glu Glu Glu Arg Ala	
	275 280 285	
45	TTG TTT TAT GCG GCA GAG ATC CTC TGC GGC TTA GAA GAC CTC CAC CGT	912
	Leu Phe Tyr Ala Ala Glu Ile Leu Cys Gly Leu Glu Asp Leu His Arg	
	290 295 300	
50	GAG AAC ACC GTC TAC CGA GAT CTG AAA CCT GAA AAC ATC CTG TTA GAT	960
	Glu Asn Thr Val Tyr Arg Asp Leu Lys Pro Glu Asn Ile Leu Leu Asp	
	305 310 315 320	
55	GAT TAT GGC CAC ATT AGG ATC TCA GAC CTG GGC TTG GCT GTG AAG ATC	1008
	Asp Tyr Gly His Ile Arg Ile Ser Asp Leu Gly Leu Ala Val Lys Ile	
	325 330 335	
60	CCC GAG GGA GAC CTG ATC CGC GGC CGG GTG GGC ACT GTT GGC TAC ATG	1056
	Pro Glu Gly Asp Leu Ile Arg Gly Arg Val Gly Thr Val Gly Tyr Met	
	340 345 350	
65	TGG GGC CTT GGC TGC CTC ATC TAT GAG ATG ATC GAG GGC CAG TCG CCG	1152
	Trp Gly Leu Gly Cys Leu Ile Tyr Glu Met Ile Glu Gly Gln Ser Pro	
	370 375 380	

129

5	TTC CGC GGC CGT AAG GAG AAG GTG AAG CGG GAG GAG GTG GAC CGC CGG	1200
	Phe Arg Gly Arg Lys Glu Lys Val Lys Arg Glu Glu Val Asp Arg Arg	
	385 390 395 400	
10	GTC CTG GAG ACG GAG GAG GTG TAC TCC CAC AAG TTC TCC GAG GAG GCC	1248
	Val Leu Glu Thr Glu Glu Val Tyr Ser His Lys Phe Ser Glu Glu Ala	
	405 410 415	
15	AAG TCC ATC TGC AAG ATG CTG CTC ACG AAA GAT GCG AAG CAG AGG CTG	1296
	Lys Ser Ile Cys Lys Met Leu Leu Thr Lys Asp Ala Lys Gln Arg Leu	
	420 425 430	
20	GGC TGC CAG GAC GAG GGG GCT GCA GAG GTC AAG AGA CAC CCC TTC TTC	1344
	Gly Cys Gln Glu Glu Gly Ala Ala Glu Val Lys Arg His Pro Phe Phe	
	435 440 445	
25	AGG AAC ATG AAC TTC AAG CGC TTA GAA GCC GGG ATG TTG GAC CCT CCC	1392
	Arg Asn Met Asn Phe Lys Arg Leu Glu Ala Gly Met Leu Asp Pro Pro	
	450 455 460	
30	TTC GTT CCA GAC CCC CGC GCT GTG TAC TGT AAG GAC GTG CTG GAC ATC	1440
	Phe Val Pro Asp Pro Arg Ala Val Tyr Cys Lys Asp Val Leu Asp Ile	
	465 470 475 480	
35	GAG CAG TTC TCC ACT GTG AAG GGC GTC AAT CTG GAC CAC ACA GAC GAC	1488
	Glu Gln Phe Ser Thr Val Lys Gly Val Asn Leu Asp His Thr Asp Asp	
	485 490 495	
40	GAC TTC TAC TCC AAG TTC TCC ACG GGC TCT GTG TCC ATC CCA TGG CAA	1536
	Asp Phe Tyr Ser Lys Phe Ser Thr Gly Ser Val Ser Ile Pro Trp Gln	
	500 505 510	
45	AAC GAG ATG ATA GAA ACA GAA TGC TTT AAG GAG CTG AAC GTG TTT GGA	1584
	Asn Glu Met Ile Glu Thr Glu Cys Phe Lys Glu Leu Asn Val Phe Gly	
	515 520 525	
50	CCT AAT GGT ACC CTC CCG CCA GAT CTG AAC AGA AAC CAC CCT CCG GAA	1632
	Pro Asn Gly Thr Leu Pro Pro Asp Leu Asn Arg Asn His Pro Pro Glu	
	530 535 540	
55	CCG CCC AAG AAA GGG CTG CTC CAG AGA CTC TTC AAG CGG CAG CAT CAG	1680
	Pro Pro Lys Lys Gly Leu Leu Gln Arg Leu Phe Lys Arg Gln His Gln	
	545 550 555 560	
60	AAC AAT TCC AAG AGT TCG CCC AGC TCC AAG ACC AGT TTT AAC CAC CAC	1728
	Asn Asn Ser Lys Ser Ser Pro Ser Ser Lys Thr Ser Phe Asn His His	
	565 570 575	
65	CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG	1824
	Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly	
	585 590 595 600	

130

5	GTG	GTG	CCC	ATC	CTG	GTC	GAG	CTG	GAC	GGC	GAC	GTA	AAC	GGC	CAC	AAG	1872
	Val	Val	Pro	Ile	Leu	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	
	610						615					620					
10	TTC	AGC	GTG	TCC	GGC	GAG	GGC	GAG	GGC	GAT	GCC	ACC	TAC	GGC	AAG	CTG	1920
	Phe	Ser	Val	Ser	Gly	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	
	625					630					635					640	
15	ACC	CTG	AAG	TTC	ATC	TGC	ACC	ACC	GGC	AAG	CTG	CCC	GTG	CCC	TGG	CCC	1968
	Thr	Leu	Lys	Phe	Ile	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	
					645					650					655		
20	ACC	CTC	GTG	ACC	ACC	CTG	ACC	TAC	GGC	GTG	CAG	TGC	TTC	AGC	CGC	TAC	2016
	Thr	Leu	Val	Thr	Thr	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	
				660					665					670			
25	CCC	GAC	CAC	ATG	AAG	CAG	CAC	GAC	TTC	TTC	AAG	TCC	GCC	ATG	CCC	GAA	2064
	Pro	Asp	His	Met	Lys	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	
			675					680					685				
30	GGC	TAC	GTC	CAG	GAG	CGC	ACC	ATC	TTC	TTC	AAG	GAC	GAC	GGC	AAC	TAC	2112
	Gly	Tyr	Val	Gln	Glu	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	
	690					695						700					
35	AAG	ACC	CGC	GCC	GAG	GTG	AAG	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	CGC	2160
	Lys	Thr	Arg	Ala	Glu	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	
	705				710					715					720		
40	ATC	GAG	CTG	AAG	GGC	ATC	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	2208
	Ile	Glu	Leu	Lys	Gly	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	
					725					730					735		
45	CAC	AAG	CTG	GAG	TAC	AAC	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	2256
	His	Lys	Leu	Glu	Tyr	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	
				740					745					750			
50	GAC	AAG	CAG	AAG	AAC	GGC	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	2304
	Asp	Lys	Gln	Lys	Asn	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	
			755					760					765				
55	ATC	GAG	GAC	GGC	AGC	GTG	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	2352
	Ile	Glu	Asp	Gly	Ser	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	
	770					775						780					
60	CCC	ATC	GGC	GAC	GGC	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	2400
	Pro	Ile	Gly	Asp	Gly	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	
	785					790					795						
65	GTG	GTG	CTG	GAG	TTC	GTG	ACC	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	2496
	Val	Leu	Leu	Glu	Phe	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	
				820					825								

GAG CTG TAC AAG TAA

Glu Leu Tyr Lys

835

2511

5

(2) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 836 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

20 Met Glu Leu Glu Asn Ile Val Ala Asn Thr Val Leu Leu Lys Ala Arg
 1 5 10 15
 Glu Gly Gly Gly Gly Lys Arg Lys Gly Lys Ser Lys Lys Trp Lys Glu
 20 25 30
 Ile Leu Lys Phe Pro His Ile Ser Gln Cys Glu Asp Leu Arg Arg Thr
 25 35 40 45
 Ile Asp Arg Asp Tyr Cys Ser Leu Cys Asp Lys Gln Pro Ile Gly Arg
 50 55 60
 Leu Leu Phe Arg Gln Phe Cys Glu Thr Arg Pro Gly Leu Glu Cys Tyr
 65 70 75 80
 30 Ile Gln Phe Leu Asp Ser Val Ala Glu Tyr Glu Val Thr Pro Asp Glu
 85 90 95
 Lys Leu Gly Glu Lys Gly Lys Glu Ile Met Thr Lys Tyr Leu Thr Pro
 100 105 110
 Lys Ser Pro Val Phe Ile Ala Gln Val Gly Gln Asp Leu Val Ser Gln
 35 115 120 125
 Thr Glu Glu Lys Leu Leu Gln Lys Pro Cys Lys Glu Leu Phe Ser Ala
 130 135 140
 Cys Ala Gln Ser Val His Glu Tyr Leu Arg Gly Glu Pro Phe His Glu
 145 150 155 160
 40 Tyr Leu Asp Ser Met Phe Phe Asp Arg Phe Leu Gln Trp Lys Trp Leu
 165 170 175
 Glu Arg Gln Pro Val Thr Lys Asn Thr Phe Arg Gln Tyr Arg Val Leu
 180 185 190
 Gly Lys Gly Gly Phe Gly Glu Val Cys Ala Cys Gln Val Arg Ala Thr
 45 195 200 205
 Gly Lys Met Tyr Ala Cys Lys Arg Leu Glu Lys Lys Arg Ile Lys Lys
 210 215 220
 Arg Lys Gly Glu Ser Met Ala Leu Asn Glu Lys Gln Ile Leu Glu Lys
 225 230 235
 240 245 250 255 260 265 270 275 280 285
 55 Phe His Ile Tyr Asn Met Gly Asn Pro Gly Phe Glu Glu Glu Arg Ala
 275 280 285
 Leu Phe Tyr Ala Ala Glu Ile Leu Cys Gly Leu Glu Asp Leu Lys Lys

	290					295						300					
	Glu	Asn	Thr	Val	Tyr	Arg	Asp	Leu	Lys	Pro	Glu	Asn	Ile	Leu	Leu	Asp	
	305					310					315					320	
5	Asp	Tyr	Gly	His	Ile	Arg	Ile	Ser	Asp	Leu	Gly	Leu	Ala	Val	Lys	Ile	
					325					330					335		
	Pro	Glu	Gly	Asp	Leu	Ile	Arg	Gly	Arg	Val	Gly	Thr	Val	Gly	Tyr	Met	
				340					345					350			
	Ala	Pro	Glu	Val	Leu	Asn	Asn	Gln	Arg	Tyr	Gly	Leu	Ser	Pro	Asp	Tyr	
			355				360						365				
10	Trp	Gly	Leu	Gly	Cys	Leu	Ile	Tyr	Glu	Met	Ile	Glu	Gly	Gln	Ser	Pro	
	370						375					380					
	Phe	Arg	Gly	Arg	Lys	Glu	Lys	Val	Lys	Arg	Glu	Glu	Val	Asp	Arg	Arg	
	385					390					395				400		
15	Val	Leu	Glu	Thr	Glu	Glu	Val	Tyr	Ser	His	Lys	Phe	Ser	Glu	Glu	Ala	
					405					410					415		
	Lys	Ser	Ile	Cys	Lys	Met	Leu	Leu	Thr	Lys	Asp	Ala	Lys	Gln	Arg	Leu	
				420					425					430			
	Gly	Cys	Gln	Glu	Glu	Gly	Ala	Ala	Glu	Val	Lys	Arg	His	Pro	Phe	Phe	
			435				440						445				
20	Arg	Asn	Met	Asn	Phe	Lys	Arg	Leu	Glu	Ala	Gly	Met	Leu	Asp	Pro	Pro	
	450						455					460					
	Phe	Val	Pro	Asp	Pro	Arg	Ala	Val	Tyr	Cys	Lys	Asp	Val	Leu	Asp	Ile	
	465					470					475				480		
25	Glu	Gln	Phe	Ser	Thr	Val	Lys	Gly	Val	Asn	Leu	Asp	His	Thr	Asp	Asp	
					485				490						495		
	Asp	Phe	Tyr	Ser	Lys	Phe	Ser	Thr	Gly	Ser	Val	Ser	Ile	Pro	Trp	Gln	
				500					505					510			
	Asn	Glu	Met	Ile	Glu	Thr	Glu	Cys	Phe	Lys	Glu	Leu	Asn	Val	Phe	Gly	
			515				520						525				
30	Pro	Asn	Gly	Thr	Leu	Pro	Pro	Asp	Leu	Asn	Arg	Asn	His	Pro	Pro	Glu	
	530						535					540					
	Pro	Pro	Lys	Lys	Gly	Leu	Leu	Gln	Arg	Leu	Phe	Lys	Arg	Gln	His	Gln	
	545					550					555					560	
35	Asn	Asn	Ser	Lys	Ser	Ser	Pro	Ser	Ser	Lys	Thr	Ser	Phe	Asn	His	His	
				565						570					575		
	Ile	Asn	Ser	Asn	His	Val	Ser	Ser	Asn	Ser	Thr	Gly	Ser	Ser	Arg	Asp	
				580					585					590			
	Pro	Pro	Val	Ala	Thr	Met	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	
			595				600						605				
40	Val	Val	Pro	Ile	Leu	Val	Glu	Leu	Asp	Gly	Asp						

133

740 745 750
 Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
 755 760 765
 Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
 5 770 775 780
 Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
 785 790 795 800
 Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
 805 810 815
 10 Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
 820 825 830
 Glu Leu Tyr Lys
 835

15 (2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1893 base pairs

(B) TYPE: nucleic acid

20 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

25

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...1890

(D) OTHER INFORMATION:

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

ATG AGC AGA AGC AAG CGT GAC AAC AAT TTT TAT AGT GTA GAG ATT GGA 48
 Met Ser Arg Ser Lys Arg Asp Asn Asn Phe Tyr Ser Val Glu Ile Gly
 1 5 10 15
 35 GAT TCT ACA TTC ACA GTC CTG AAA CGA TAT CAG AAT TTA AAA CCT ATA 96
 Asp Ser Thr Phe Thr Val Leu Lys Arg Tyr Gln Asn Leu Lys Pro Ile
 20 25 30
 40 GGC TCA GGA GCT CAA GGA ATA GTA TGC GCA GCT TAT GAT GCC ATT CTT 144
 Gly Ser Gly Ala Gln Gly Ile Val Cys Ala Ala Tyr Asp Ala Ile Leu
 35 40 45
 45 GAA AGA AAT GTT GCA ATC AAG AAG CTA AGC CGA CCA TTT CAG AAT CAG 192
 Glu Arg Asn Val Ala Ile Lys Lys Leu Ser Arg Pro Phe Gln Asn Gln
 50 55 60
 ACT CAT GCC AAG CGG GCC TAC AGA GAG CTA GTT CTT ATG AAA TGT GTT 240
 Thr His Ala Lys Arg Ala Thr Val
 85 90 95
 55 TCC CTA GAA GAA TTT CAA GAT GTT TAC ATA GTC ATG GAG CTC ATG GAT

	Ser	Leu	Glu	Glu	Phe	Gln	Asp	Val	Tyr	Ile	Val	Met	Glu	Leu	Met	Asp	
	100								105				110				
5	GCA	AAT	CTT	TGC	CAA	GTG	ATT	CAG	ATG	GAG	CTA	GAT	CAT	GAA	AGA	ATG	384
	Ala	Asn	Leu	Cys	Gln	Val	Ile	Gln	Met	Glu	Leu	Asp	His	Glu	Arg	Met	
	115				120				125								
10	TCC	TAC	CTT	CTC	TAT	CAG	ATG	CTG	TGT	GGA	ATC	AAG	CAC	CTT	CAT	TCT	432
	Ser	Tyr	Leu	Leu	Tyr	Gln	Met	Leu	Cys	Gly	Ile	Lys	His	Leu	His	Ser	
	130				135				140								
15	GCT	GGA	ATT	ATT	CAT	CGG	GAC	TTA	AAG	CCC	AGT	AAT	ATA	GTA	GTA	AAA	480
	Ala	Gly	Ile	Ile	His	Arg	Asp	Leu	Lys	Pro	Ser	Asn	Ile	Val	Val	Lys	
	145				150				155				160				
20	TCT	GAT	TGC	ACT	TTG	AAG	ATT	CTT	GAC	TTC	GGT	CTG	GCC	AGG	ACT	GCA	528
	Ser	Asp	Cys	Thr	Leu	Lys	Ile	Leu	Asp	Phe	Gly	Leu	Ala	Arg	Thr	Ala	
	165				170				175								
25	GGA	ACG	AGT	TTT	ATG	ATG	ACG	CCT	TAT	GTA	GTG	ACT	CGC	TAC	TAC	AGA	576
	Gly	Thr	Ser	Phe	Met	Met	Thr	Pro	Tyr	Val	Val	Thr	Arg	Tyr	Tyr	Arg	
	180				185				190								
30	GCA	CCC	GAG	GTC	ATC	CTT	GGC	ATG	GGC	TAC	AAG	GAA	AAC	GTG	GAT	TTA	624
	Ala	Pro	Glu	Val	Ile	Leu	Gly	Met	Gly	Tyr	Lys	Glu	Asn	Val	Asp	Leu	
	195				200				205								
35	TGG	TCT	GTG	GGG	TGC	ATT	ATG	GGA	GAA	ATG	GTT	TGC	CAC	AAA	ATC	CTC	672
	Trp	Ser	Val	Gly	Cys	Ile	Met	Gly	Glu	Met	Val	Cys	His	Lys	Ile	Leu	
	210				215				220								
40	TTT	CCA	GGA	AGG	GAC	TAT	ATT	GAT	CAG	TGG	AAT	AAA	GTT	ATT	GAA	CAG	720
	Phe	Pro	Gly	Arg	Asp	Tyr	Ile	Asp	Gln	Trp	Asn	Lys	Val	Ile	Glu	Gln	
	225				230				235				240				
45	CTT	GGA	ACA	CCA	TGT	CCT	GAA	TTC	ATG	AAG	AAA	CTG	CAA	CCA	ACA	GTA	768
	Leu	Gly	Thr	Pro	Cys	Pro	Glu	Phe	Met	Lys	Lys	Leu	Gln	Pro	Thr	Val	
	245				250				255								
50	AGG	ACT	TAC	GTT	GAA	AAC	AGA	CCT	AAA	TAT	GCT	GGA	TAT	AGC	TTT	GAG	816
	Arg	Thr	Tyr	Val	Glu	Asn	Arg	Pro	Lys	Tyr	Ala	Gly	Tyr	Ser	Phe	Glu	
	260				265				270								
55	AAA	CTC	TTC	CCT	GAT	GTC	CTT	TTC	CCA	GCT	GAC	TCA	GAA	CAC	AAC	AAA	864
	Lys	Leu	Phe	Pro	Asp	Val	Leu	Phe	Pro	Ala	Asp	Ser	Glu	His	Asn	Lys	
	275				280				285								
60	CTT	AAA	GCC	AGT	CAG	GCA	AGG	GAT	TTG	TTA	TCC	AAA	ATG	CTG	GTA	ATA	912
	Leu	Lys	Ala	Ser	Gln	Ala	Arg	Asp	Glu	Ala	Leu	Gln	His	Pro	Tyr		
	305				310				315				320				
65	ATC	AAT	GTC	TGG	TAT	GAT	CCT	TCT	GAA	GCA	GAA	GCT	GCA	GCA	GCA	AAA	960
	Ile	Asn	Gly	Trp	Tyr	Asp	Pro	Ser	Glu	Ala	Leu	Gln	His	Pro	Tyr		
	305				310				315				320				

Ile Asn Val Trp Tyr Asp Pro Ser Glu Ala Glu Ala Pro Pro Pro Lys
325 330 335

530

535

540

55

ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC GAG

136

Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg
 545 550 555 560

5 CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG 1728
 His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln
 565 570 575

10 AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC 1776
 Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr
 580 585 590

15 CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT 1824
 Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp
 595 600 605

CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC 1872
 His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly
 610 615 620

20 ATG GAC GAG CTG TAC AAG TAA 1893
 Met Asp Glu Leu Tyr Lys
 625 630

25 (2) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 630 amino acids
 (B) TYPE: amino acid
 30 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

Met Ser Arg Ser Lys Arg Asp Asn Asn Phe Tyr Ser Val Glu Ile Gly
 1 5 10 15

40 Asp Ser Thr Phe Thr Val Leu Lys Arg Tyr Gln Asn Leu Lys Pro Ile
 20 25 30

Gly Ser Gly Ala Gln Gly Ile Val Cys Ala Ala Tyr Asp Ala Ile Leu
 35 40 45

45 Glu Arg Asn Val Ala Ile Lys Lys Leu Ser Arg Pro Phe Gln Asn Gln
 50 55 60

Thr His Ala Lys Arg Ala Tyr Arg Glu Leu Val Leu Met Lys Cys Val
 65 70 75 80

Asn His Lys Asn Ile Ile Gly Leu Leu Asn Val Phe Thr Pro Gln Lys
 85 90 95 100 105 110 115 120 125

55 Ser Tyr Leu Leu Tyr Gln Met Leu Cys Gly Ile Lys His Leu His Ser
 130 135 140

Ala Gly Ile Ile His Arg Asp Leu Lys Pro Ser Asn Ile Thr Met Lys
 145 150 155 160 165 170 175 180 185 190 195 200

	145					150					155					160
	Ser	Asp	Cys	Thr	Leu	Lys	Ile	Leu	Asp	Phe	Gly	Leu	Ala	Arg	Thr	Ala
					165					170						175
5	Gly	Thr	Ser	Phe	Met	Met	Thr	Pro	Tyr	Val	Val	Thr	Arg	Tyr	Tyr	Arg
				180					185							190
	Ala	Pro	Glu	Val	Ile	Leu	Gly	Met	Gly	Tyr	Lys	Glu	Asn	Val	Asp	Leu
			195					200					205			
	Trp	Ser	Val	Gly	Cys	Ile	Met	Gly	Glu	Met	Val	Cys	His	Lys	Ile	Leu
		210					215					220				
10	Phe	Pro	Gly	Arg	Asp	Tyr	Ile	Asp	Gln	Trp	Asn	Lys	Val	Ile	Glu	Gln
	225					230					235					240
	Leu	Gly	Thr	Pro	Cys	Pro	Glu	Phe	Met	Lys	Lys	Leu	Gln	Pro	Thr	Val
				245						250					255	
15	Arg	Thr	Tyr	Val	Glu	Asn	Arg	Pro	Lys	Tyr	Ala	Gly	Tyr	Ser	Phe	Glu
				260					265						270	
	Lys	Leu	Phe	Pro	Asp	Val	Leu	Phe	Pro	Ala	Asp	Ser	Glu	His	Asn	Lys
			275					280					285			
	Leu	Lys	Ala	Ser	Gln	Ala	Arg	Asp	Leu	Leu	Ser	Lys	Met	Leu	Val	Ile
		290					295					300				
20	Asp	Ala	Ser	Lys	Arg	Ile	Ser	Val	Asp	Glu	Ala	Leu	Gln	His	Pro	Tyr
	305					310					315					320
	Ile	Asn	Val	Trp	Tyr	Asp	Pro	Ser	Glu	Ala	Glu	Ala	Pro	Pro	Pro	Lys
				325						330					335	
25	Ile	Pro	Asp	Lys	Gln	Leu	Asp	Glu	Arg	Glu	His	Thr	Ile	Glu	Glu	Trp
			340						345					350		
	Lys	Glu	Leu	Ile	Tyr	Lys	Glu	Val	Met	Asp	Leu	Glu	Glu	Arg	Thr	Lys
			355					360					365			
	Asn	Gly	Val	Ile	Arg	Gly	Gln	Pro	Ser	Pro	Leu	Ala	Gln	Val	Gln	Gln
		370					375					380				
30	Trp	Asp	Pro	Pro	Val	Ala	Thr	Met	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe
	385					390					395					400
	Thr	Gly	Val	Val	Pro	Ile	Leu	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly
				405						410					415	
35	His	Lys	Phe	Ser	Val	Ser	Gly	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly
			420						425					430		
	Lys	Leu	Thr	Leu	Lys	Phe	Ile	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro
			435					440					445			
	Trp	Pro	Thr	Leu	Val	Thr	Thr	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser
		450					455					460				
40	Arg	Tyr	Pro	Asp	His	Met	Lys	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met
	465					470					475					480
	Pro	Glu	Gly	Tyr	Val	Gln	Glu									

138

595 600 605
 His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly
 610 615 620
 Met Asp Glu Leu Tyr Lys
 5 625 630

(2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:

- 10 (A) LENGTH: 1821 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- 20 (A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...1818
 (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

25 ATG TCT CAG GAG AGG CCC ACG TTC TAC CGG CAG GAG CTG AAC AAG ACA 48
 Met Ser Gln Glu Arg Pro Thr Phe Tyr Arg Gln Glu Leu Asn Lys Thr
 1 5 10 15
 30 ATC TGG GAG GTG CCC GAG CGT TAC CAG AAC CTG TCT CCA GTG GGC TCT 96
 Ile Trp Glu Val Pro Glu Arg Tyr Gln Asn Leu Ser Pro Val Gly Ser
 20 25 30
 35 GGC GCC TAT GGC TCT GTG TGT GCT GCT TTT GAC ACA AAA ACG GGG TTA 144
 Gly Ala Tyr Gly Ser Val Cys Ala Ala Phe Asp Thr Lys Thr Gly Leu
 35 40 45
 40 CGT GTG GCA GTG AAG AAG CTC TCC AGA CCA TTT CAG TCC ATC ATT CAT 192
 Arg Val Ala Val Lys Lys Leu Ser Arg Pro Phe Gln Ser Ile Ile His
 50 55 60
 45 GCG AAA AGA ACC TAC AGA GAA CTG CGG TTA CTT AAA CAT ATG AAA CAT 240
 Ala Lys Arg Thr Tyr Arg Glu Leu Arg Leu Leu Lys His Met Lys His
 65 70 75 80
 50 GAA AAT GTG ATT GGT CTG TTG GAC GTT TTT ACA CCT GCA AGG TCT CTG 288
 Glu Asn Val Ile Gly Leu Leu Asp Val Phe Thr Pro Ala Arg Ser Leu
 85 90 95
 55 GAG GAA TTC AAT GAT GTG TAT CTG GTG ACC CAT CTC ATG GGG GCA GAT 336
 Glu Glu Phe Asn Asn Val Thr
 115 120 125
 60 TTC CTT ATC TAC CAA ATT CTC CGA GGT CTA AAG TAT ATA CAT TCA GGT 384

	Phe	Leu	Ile	Tyr	Gln	Ile	Leu	Arg	Gly	Leu	Lys	Tyr	Ile	His	Ser	Ala	
	130						135						140				
5	GAC	ATA	ATT	CAC	AGG	GAC	CTA	AAA	CCT	AGT	AAT	CTA	GCT	GTG	AAT	GAA	480
	Asp	Ile	Ile	His	Arg	Asp	Leu	Lys	Pro	Ser	Asn	Leu	Ala	Val	Asn	Glu	
	145					150					155					160	
10	GAC	TGT	GAG	CTG	AAG	ATT	CTG	GAT	TTT	GGA	CTG	GCT	CGG	CAC	ACA	GAT	528
	Asp	Cys	Glu	Leu	Lys	Ile	Leu	Asp	Phe	Gly	Leu	Ala	Arg	His	Thr	Asp	
					165					170						175	
15	GAT	GAA	ATG	ACA	GGC	TAC	GTG	GCC	ACT	AGG	TGG	TAC	AGG	GCT	CCT	GAG	576
	Asp	Glu	Met	Thr	Gly	Tyr	Val	Ala	Thr	Arg	Trp	Tyr	Arg	Ala	Pro	Glu	
					180					185					190		
20	ATC	ATG	CTG	AAC	TGG	ATG	CAT	TAC	AAC	CAG	ACA	GTT	GAT	ATT	TGG	TCA	624
	Ile	Met	Leu	Asn	Trp	Met	His	Tyr	Asn	Gln	Thr	Val	Asp	Ile	Trp	Ser	
				195					200					205			
25	GTG	GGA	TGC	ATA	ATG	GCC	GAG	CTG	TTG	ACT	GGA	AGA	ACA	TTG	TTT	CCT	672
	Val	Gly	Cys	Ile	Met	Ala	Glu	Leu	Leu	Thr	Gly	Arg	Thr	Leu	Phe	Pro	
		210					215						220				
30	GGT	ACA	GAC	CAT	ATT	GAT	CAG	TTG	AAG	CTC	ATT	TTA	AGA	CTC	GTT	GGA	720
	Gly	Thr	Asp	His	Ile	Asp	Gln	Leu	Lys	Leu	Ile	Leu	Arg	Leu	Val	Gly	
						230					235					240	
35	ACC	CCA	GGG	GCT	GAG	CTT	TTG	AAG	AAA	ATC	TCC	TCA	GAG	TCT	GCA	AGA	768
	Thr	Pro	Gly	Ala	Glu	Leu	Leu	Lys	Lys	Ile	Ser	Ser	Glu	Ser	Ala	Arg	
					245					250						255	
40	AAC	TAT	ATT	CAG	TCT	TTG	ACT	CAG	ATG	CCG	AAG	ATG	AAC	TTT	GCG	AAT	816
	Asn	Tyr	Ile	Gln	Ser	Leu	Thr	Gln	Met	Pro	Lys	Met	Asn	Phe	Ala	Asn	
				260						265					270		
45	GTA	TTT	ATT	GGT	GCC	AAT	CCC	CTG	GCT	GTC	GAC	TTG	CTG	GAG	AAG	ATG	864
	Val	Phe	Ile	Gly	Ala	Asn	Pro	Leu	Ala	Val	Asp	Leu	Leu	Glu	Lys	Met	
				275				280						285			
50	CTT	GTA	TTG	GAC	TCA	GAT	AAG	AGA	ATT	ACA	GCG	GCC	CAA	GCC	CTT	GCA	912
	Leu	Val	Leu	Asp	Ser	Asp	Lys	Arg	Ile	Thr	Ala	Ala	Gln	Ala	Leu	Ala	
		290					295						300				
55	CAT	GCC	TAC	TTT	GCT	CAG	TAC	CAC	GAT	CCT	GAT	GAT	GAA	CCA	GTG	GCC	960
	His	Ala	Tyr	Phe	Ala	Gln	Tyr	His	Asp	Pro	Asp	Asp	Glu	Pro	Val	Ala	
		305				310					315					320	
60	GAT	CCT	TAT	GAT	CAG	TCC	TTT	GAA	AGC	AGG	GAC	CTC	CTT	ATA	GAT	GAG	1008
	Asp	Pro	Tyr	Asp	Gln	Ser	Phe	Glu	Ser	Arg	Leu	Leu	Leu	Leu	Leu	Leu	

140

	Leu	Asp	Gln	Glu	Glu	Met	Glu	Ser	Glu	Asp	Pro	Pro	Val	Ala	Thr	Met	
			355					360					365				
5	GTG	AGC	AAG	GGC	GAG	GAG	CTG	TTC	ACC	GGG	GTG	GTG	CCC	ATC	CTG	GTC	1152
	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	Val	
			370				375					380					
10	GAG	CTG	GAC	GGC	GAC	GTA	AAC	GGC	CAC	AAG	TTC	AGC	GTG	TCC	GGC	GAG	1200
	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	Glu	
			385				390				395					400	
15	GGC	GAG	GGC	GAT	GCC	ACC	TAC	GGC	AAG	CTG	ACC	CTG	AAG	TTC	ATC	TGC	1248
	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	Cys	
					405					410					415		
	ACC	ACC	GGC	AAG	CTG	CCC	GTG	CCC	TGG	CCC	ACC	CTC	GTG	ACC	ACC	CTG	1296
	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	Leu	
				420					425					430			
20	ACC	TAC	GGC	GTG	CAG	TGC	TTC	AGC	CGC	TAC	CCC	GAC	CAC	ATG	AAG	CAG	1344
	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	Gln	
			435					440					445				
25	CAC	GAC	TTC	TTC	AAG	TCC	GCC	ATG	CCC	GAA	GGC	TAC	GTC	CAG	GAG	CGC	1392
	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	Arg	
		450					455					460					
30	ACC	ATC	TTC	TTC	AAG	GAC	GAC	GGC	AAC	TAC	AAG	ACC	CGC	GCC	GAG	GTG	1440
	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	Val	
		465				470					475				480		
35	AAG	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	CGC	ATC	GAG	CTG	AAG	GGC	ATC	1488
	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	Ile	
				485						490					495		
	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	CAC	AAG	CTG	GAG	TAC	AAC	1536
	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	Asn	
				500					505					510			
40	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	GAC	AAG	CAG	AAG	AAC	GGC	1584
	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	Gly	
			515					520					525				
45	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	ATC	GAG	GAC	GGC	AGC	GTG	1632
	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	Val	
		530					535					540					
55	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	CCC	ATC	GGC	GAC	GGC	GGC	1680
	Gln	Leu	Ala	Asp	His	Thr	Val	Val	Val	Val	Val	Val	Val	Val	Val	Val	
							565					570			575		
	AAA	GAC	CCC	AAC	GAG	AAG	CCC	GAT	CAC	ATG	GTG	GTG	GTG	GTG	GTG	GTG	

141

Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
 580 585 590

ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA 1821
 5 Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
 595 600 605

(2) INFORMATION FOR SEQ ID NO:65:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 606 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

15

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

Met Ser Gln Glu Arg Pro Thr Phe Tyr Arg Gln Glu Leu Asn Lys Thr
 1 5 10 15
 Ile Trp Glu Val Pro Glu Arg Tyr Gln Asn Leu Ser Pro Val Gly Ser
 25 20 25 30
 Gly Ala Tyr Gly Ser Val Cys Ala Ala Phe Asp Thr Lys Thr Gly Leu
 35 40 45
 Arg Val Ala Val Lys Lys Leu Ser Arg Pro Phe Gln Ser Ile Ile His
 50 55 60
 30 Ala Lys Arg Thr Tyr Arg Glu Leu Arg Leu Leu Lys His Met Lys His
 65 70 75 80
 Glu Asn Val Ile Gly Leu Leu Asp Val Phe Thr Pro Ala Arg Ser Leu
 85 90 95
 Glu Glu Phe Asn Asp Val Tyr Leu Val Thr His Leu Met Gly Ala Asp
 35 100 105 110
 Leu Asn Asn Ile Val Lys Cys Gln Lys Leu Thr Asp Asp His Val Gln
 115 120 125
 Phe Leu Ile Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala
 130 135 140
 40 Asp Ile Ile His Arg Asp Leu Lys Pro Ser Asn Leu Ala Val Asn Glu
 145 150 155 160
 Asp Cys Glu Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg His Thr Asp
 165 170 175
 Asp Glu Met Thr Gly Tyr Val Ala Thr Arg Trp Tyr Arg Ala Pro Glu
 45 180 185 190
 Ile Met Leu Asn Trp Met His Tyr Asn Gln Thr Val Asp Ile Trp Ser
 195 200 205
 Val Gly Cys Ile Met Ala Glu Leu Leu Thr Gly Arg Thr Leu Phe Pro
 210 215 220
 225 230 235 240 245 250 255
 55 Asn Tyr Ile Gln Ser Leu Thr Gln Met Pro Lys Met Asn Phe Ala Asn
 260 265 270
 Val Phe Ile Gly Ala Asn Pro Leu Ala Val Asn Leu Leu Glu Thr Met

142

	275		280		285
	Leu Val Leu Asp Ser Asp	Lys Arg Ile Thr Ala	Ala Gln Ala Leu Ala		
	290	295	300		
5	His Ala Tyr Phe Ala Gln Tyr His Asp Pro Asp Asp Glu Pro Val Ala				
	305	310	315		320
	Asp Pro Tyr Asp Gln Ser Phe Glu Ser Arg Asp Leu Leu Ile Asp Glu				
		325	330		335
	Trp Lys Ser Leu Thr Tyr Asp Glu Val Ile Ser Phe Val Pro Pro Pro				
		340	345		350
10	Leu Asp Gln Glu Glu Met Glu Ser Glu Asp Pro Pro Val Ala Thr Met				
		355	360		365
	Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val				
		370	375		380
	Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu				
15		385	390		395
	Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys				
		405	410		415
	Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu				
		420	425		430
20	Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln				
		435	440		445
	His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg				
		450	455		460
	Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val				
25		465	470		475
	Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile				
		485	490		495
	Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn				
		500	505		510
30	Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly				
		515	520		525
	Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val				
		530	535		540
	Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro				
35		545	550		555
	Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser				
		565	570		575
	Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val				
		580	585		590
40	Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys				
		595	600		605

(2) INFORMATION FOR SEQ ID NO:66:

45

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2913 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

55

- (A) NAME/KEY: Coding Sequence
- (B) LOCATION: 1...2910
- (D) OTHER INFORMATION:

143

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

5	ATG AGT GCT GAG GGG TAC CAG TAC AGA GCG CTG TAT GAT TAT AAA AAG	48
	Met Ser Ala Glu Gly Tyr Gln Tyr Arg Ala Leu Tyr Asp Tyr Lys Lys	
	1 5 10 15	
10	GAA AGA GAA GAA GAT ATT GAC TTG CAC TTG GGT GAC ATA TTG ACT GTG	96
	Glu Arg Glu Glu Asp Ile Asp Leu His Leu Gly Asp Ile Leu Thr Val	
	20 25 30	
15	AAT AAA GGG TCC TTA GTA GCT CTT GGA TTC AGT GAT GGA CAG GAA GCC	144
	Asn Lys Gly Ser Leu Val Ala Leu Gly Phe Ser Asp Gly Gln Glu Ala	
	35 40 45	
20	AGG CCT GAA GAA ATT GGC TGG TTA AAT GGC TAT AAT GAA ACC ACA GGG	192
	Arg Pro Glu Glu Ile Gly Trp Leu Asn Gly Tyr Asn Glu Thr Thr Gly	
	50 55 60	
25	GAA AGG GGG GAC TTT CCG GGA ACT TAC GTA GAA TAT ATT GGA AGG AAA	240
	Glu Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Tyr Ile Gly Arg Lys	
	65 70 75 80	
30	AAA ATC TCG CCT CCC ACA CCA AAG CCC CGG CCA CCT CGG CCT CTT CCT	288
	Lys Ile Ser Pro Pro Thr Pro Lys Pro Arg Pro Pro Arg Pro Leu Pro	
	85 90 95	
35	GTT GCA CCA GGT TCT TCG AAA ACT GAA GCA GAT GTT GAA CAA CAA GCT	336
	Val Ala Pro Gly Ser Ser Lys Thr Glu Ala Asp Val Glu Gln Glu Ala	
	100 105 110	
40	TTG ACT CTC CCG GAT CTT GCA GAG CAG TTT GCC CCT CCT GAC ATT GCC	384
	Leu Thr Leu Pro Asp Leu Ala Glu Gln Phe Ala Pro Pro Asp Ile Ala	
	115 120 125	
45	CCG CCT CTT CTT ATC AAG CTC GTG GAA GCC ATT GAA AAG AAA GGT CTG	432
	Pro Pro Leu Leu Ile Lys Leu Val Glu Ala Ile Glu Lys Lys Gly Leu	
	130 135 140	
50	GAA TGT TCA ACT CTA TAC AGA ACA CAG AGC TCC AGC AAC CTG GCA GAA	480
	Glu Cys Ser Thr Leu Tyr Arg Thr Gln Ser Ser Ser Asn Leu Ala Glu	
	145 150 155 160	
55	TTA CGA CAG CTT CTT GAT TGT GAT ACA CCC TCC GTG GAC TTG GAA ATG	528
	Leu Arg Gln Leu Leu Asp Cys Asp Thr Pro Ser Val Asp Leu Glu Met	
	165 170 175	
	ATC GAT GTG CAC GTT TTG GCT GAC GCT TTC AAA CGC TAT CTC CTG GAC	
	Ile Asp Val His Val Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr	
	180 185 190 195 200 205	
	TTA GCT CCA GAA GTA CAA AGC TCC GAA GAA TAT ATT GAC GAT GAT GAT	
	Leu Ala Val Tyr Ser Glu Met Ile Ser	
	195 200 205	

[illegible]

	Gln	Asp	Gln	Val	Val	Lys	Glu	Asp	Asn	Ile	Glu	Ala	Val	Gly	Lys	Lys			
	435						440						445						
5	TTA	CAT	GAA	TAT	AAC	ACT	CAG	TTT	CAA	GAA	AAA	AGT	CGA	GAA	TAT	GAT	1392		
	Leu	His	Glu	Tyr	Asn	Thr	Gln	Phe	Gln	Glu	Lys	Ser	Arg	Glu	Tyr	Asp			
	450						455						460						
10	AGA	TTA	TAT	GAA	GAA	TAT	ACC	CGC	ACA	TCC	CAG	GAA	ATC	CAA	ATG	AAA	1440		
	Arg	Leu	Tyr	Glu	Glu	Tyr	Thr	Arg	Thr	Ser	Gln	Glu	Ile	Gln	Met	Lys			
	465						470						475						480
15	AGG	ACA	GCT	ATT	GAA	GCA	TTT	AAT	GAA	ACC	ATA	AAA	ATA	TTT	GAA	GAA	1488		
	Arg	Thr	Ala	Ile	Glu	Ala	Phe	Asn	Glu	Thr	Ile	Lys	Ile	Phe	Glu	Glu			
	485						490						495						
20	CAG	TGC	CAG	ACC	CAA	GAG	CGG	TAC	AGC	AAA	GAA	TAC	ATA	GAA	AAG	TTT	1536		
	Gln	Cys	Gln	Thr	Gln	Glu	Arg	Tyr	Ser	Lys	Glu	Tyr	Ile	Glu	Lys	Phe			
	500						505						510						
25	AAA	CGT	GAA	GGC	AAT	GAG	AAA	GAA	ATA	CAA	AGG	ATT	ATG	CAT	AAT	TAT	1584		
	Lys	Arg	Glu	Gly	Asn	Glu	Lys	Glu	Ile	Gln	Arg	Ile	Met	His	Asn	Tyr			
	515						520						525						
30	GAT	AAG	TTG	AAG	TCT	CGA	ATC	AGT	GAA	ATT	ATT	GAC	AGT	AGA	AGA	AGA	1632		
	Asp	Lys	Leu	Lys	Ser	Arg	Ile	Ser	Glu	Ile	Ile	Asp	Ser	Arg	Arg	Arg			
	530						535						540						
35	TTG	GAA	GAA	GAC	TTG	AAG	AAG	CAG	GCA	GCT	GAG	TAT	CGA	GAA	ATT	GAC	1680		
	Leu	Glu	Glu	Asp	Leu	Lys	Lys	Gln	Ala	Ala	Glu	Tyr	Arg	Glu	Ile	Asp			
	545						550						555						560
40	AAA	CGT	ATG	AAC	AGC	ATT	AAA	CCA	GAC	CTT	ATC	CAG	CTG	AGA	AAG	ACG	1728		
	Lys	Arg	Met	Asn	Ser	Ile	Lys	Pro	Asp	Leu	Ile	Gln	Leu	Arg	Lys	Thr			
	565						570						575						
45	AGA	GAC	CAA	TAC	TTG	ATG	TGG	TTG	ACT	CAA	AAA	GGT	GTT	CGG	CAA	AAG	1776		
	Arg	Asp	Gln	Tyr	Leu	Met	Trp	Leu	Thr	Gln	Lys	Gly	Val	Arg	Gln	Lys			
	580						585						590						
50	AAG	TTG	AAC	GAG	TGG	TTG	GGC	AAT	GAA	AAC	ACT	GAA	GAC	CAA	TAT	TCA	1824		
	Lys	Leu	Asn	Glu	Trp	Leu	Gly	Asn	Glu	Asn	Thr	Glu	Asp	Gln	Tyr	Ser			
	595						600						605						
55	CTG	GTG	GAA	GAT	GAT	GAA	GAT	TTG	CCC	CAT	CAT	GAT	GAG	AAG	ACA	TGG	1872		
	Leu	Val	Glu	Asp	Asp	Glu	Asp	Leu	Pro	His	His	Asp	Glu	Lys	Thr	Trp			
	610						615						620						
60	AAT	GTT	GGA	AGC	AGC	AAC	CGA	AAC	AAA	GCT	GAA	AAC	CTG	TTG	CGA	GCG	1920		
	Asn	Val	Gly	Ser	Ser	Asn	Arg	Asn	Ala	Ser	Ser	Lys	Gln	Gly	Cys				
	645						650						655						
65	TAT	GCC	TGC	TCT	GTA	GTG	GTG	GAC	GGC	GAA	GTA	AGC	CAT	TCG	TTG	AAA	1968		
	Leu	Ala	Cys	Leu	Val	Val	Val	Arg	Glu	Ser	Ser	Lys	Gln	Gly	Cys				
	645						650						655						

[illegible]

147

Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn
 885 890 895

5 TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC 2736
 Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp
 900 905 910

10 CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC 2784
 His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro
 915 920 925

15 GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC 2832
 Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn
 930 935 940

GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG 2880
 Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly
 945 950 955 960

20 ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA 2913
 Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
 965 970

25 (2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 970 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

Met Ser Ala Glu Gly Tyr Gln Tyr Arg Ala Leu Tyr Asp Tyr Lys Lys
 1 5 10 15

40 Glu Arg Glu Glu Asp Ile Asp Leu His Leu Gly Asp Ile Leu Thr Val
 20 25 30

Asn Lys Gly Ser Leu Val Ala Leu Gly Phe Ser Asp Gly Gln Glu Ala
 35 40 45

45 Arg Pro Glu Glu Ile Gly Trp Leu Asn Gly Tyr Asn Glu Thr Thr Gly
 50 55 60

Glu Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Tyr Ile Gly Arg Lys
 65 70 75 80

Lys Ile Ser Pro Pro Thr Pro Lys Pro Arg Pro Arg Pro Leu Pro

110 120 125

55 Pro Pro Leu Leu Ile Lys Leu Val Glu Ala Ile Glu Lys Lys Gly Leu
 130 135 140

Glu Cys Ser Thr Leu Tyr Arg Thr Gln Ser Ser Ser Ser Ser Ser Ser

		145				150				155					160		
		Leu	Arg	Gln	Leu	Leu	Asp	Cys	Asp	Thr	Pro	Ser	Val	Asp	Leu	Glu	Met
						165					170					175	
5		Ile	Asp	Val	His	Val	Leu	Ala	Asp	Ala	Phe	Lys	Arg	Tyr	Leu	Leu	Asp
					180					185					190		
		Leu	Pro	Asn	Pro	Val	Ile	Pro	Ala	Ala	Val	Tyr	Ser	Glu	Met	Ile	Ser
					195				200					205			
		Leu	Ala	Pro	Glu	Val	Gln	Ser	Ser	Glu	Glu	Tyr	Ile	Gln	Leu	Leu	Lys
					210				215				220				
10		Lys	Leu	Ile	Arg	Ser	Pro	Ser	Ile	Pro	His	Gln	Tyr	Trp	Leu	Thr	Leu
		225					230					235					240
		Gln	Tyr	Leu	Leu	Lys	His	Phe	Phe	Lys	Leu	Ser	Gln	Thr	Ser	Ser	Lys
						245					250				255		
15		Asn	Leu	Leu	Asn	Ala	Arg	Val	Leu	Ser	Glu	Ile	Phe	Ser	Pro	Met	Leu
					260					265					270		
		Phe	Arg	Phe	Ser	Ala	Ala	Ser	Ser	Asp	Asn	Thr	Glu	Asn	Leu	Ile	Lys
					275				280					285			
		Val	Ile	Glu	Ile	Leu	Ile	Ser	Thr	Glu	Trp	Asn	Glu	Arg	Gln	Pro	Ala
								295					300				
20		Pro	Ala	Leu	Pro	Pro	Lys	Pro	Pro	Lys	Pro	Thr	Thr	Val	Ala	Asn	Asn
		305					310					315					320
		Gly	Met	Asn	Asn	Asn	Met	Ser	Leu	Gln	Asn	Ala	Glu	Trp	Tyr	Trp	Gly
						325					330				335		
25		Asp	Ile	Ser	Arg	Glu	Glu	Val	Asn	Glu	Lys	Leu	Arg	Asp	Thr	Ala	Asp
					340					345					350		
		Gly	Thr	Phe	Leu	Val	Arg	Asp	Ala	Ser	Thr	Lys	Met	His	Gly	Asp	Tyr
					355				360					365			
		Thr	Leu	Thr	Leu	Arg	Lys	Gly	Gly	Asn	Asn	Lys	Leu	Ile	Lys	Ile	Phe
								375					380				
30		His	Arg	Asp	Gly	Lys	Tyr	Gly	Phe	Ser	Asp	Pro	Leu	Thr	Phe	Ser	Ser
		385					390					395					400
		Val	Val	Glu	Leu	Ile	Asn	His	Tyr	Arg	Asn	Glu	Ser	Leu	Ala	Gln	Tyr
						405					410				415		
35		Asn	Pro	Lys	Leu	Asp	Val	Lys	Leu	Leu	Tyr	Pro	Val	Ser	Lys	Tyr	Gln
					420					425					430		
		Gln	Asp	Gln	Val	Val	Lys	Glu	Asp	Asn	Ile	Glu	Ala	Val	Gly	Lys	Lys
					435				440					445			
		Leu	His	Glu	Tyr	Asn	Thr	Gln	Phe	Gln	Glu	Lys	Ser	Arg	Glu	Tyr	Asp
								455					460				
40		Arg	Leu	Tyr	Glu	Glu	Tyr	Thr	Arg	Thr	Ser	Gln	Glu	Ile	Gln	Met	Lys
		465															

149

	595		600		605														
	Leu	Val	Glu	Asp	Asp	Glu	Asp	Leu	Pro	His	His	Asp	Glu	Lys	Thr	Trp			
	610						615					620							
5	Asn	Val	Gly	Ser	Ser	Asn	Arg	Asn	Lys	Ala	Glu	Asn	Leu	Leu	Arg	Gly			
	625					630						635				640			
	Lys	Arg	Asp	Gly	Thr	Phe	Leu	Val	Arg	Glu	Ser	Ser	Lys	Gln	Gly	Cys			
					645					650					655				
	Tyr	Ala	Cys	Ser	Val	Val	Val	Asp	Gly	Glu	Val	Lys	His	Cys	Val	Ile			
				660					665					670					
10	Asn	Lys	Thr	Ala	Thr	Gly	Tyr	Gly	Phe	Ala	Glu	Pro	Tyr	Asn	Leu	Tyr			
		675					680						685						
	Ser	Ser	Leu	Lys	Glu	Leu	Val	Leu	His	Tyr	Gln	His	Thr	Ser	Leu	Val			
		690					695					700							
	Gln	His	Asn	Asp	Ser	Leu	Asn	Val	Thr	Leu	Ala	Tyr	Pro	Val	Tyr	Ala			
15	705					710					715				720				
	Gln	Gln	Arg	Arg	Gln	Asp	Pro	Pro	Val	Ala	Thr	Met	Val	Ser	Lys	Gly			
					725					730					735				
	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	Val	Glu	Leu	Asp	Gly			
				740					745					750					
20	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	Glu	Gly	Glu	Gly	Asp			
		755					760						765						
	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	Cys	Thr	Thr	Gly	Lys			
		770					775					780							
	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	Leu	Thr	Tyr	Gly	Val			
25	785					790					795				800				
	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	Gln	His	Asp	Phe	Phe			
					805				810						815				
	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	Arg	Thr	Ile	Phe	Phe			
				820				825					830						
30	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	Val	Lys	Phe	Glu	Gly			
		835					840					845							
	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	Ile	Asp	Phe	Lys	Glu			
		850					855				860								
	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	Asn	Tyr	Asn	Ser	His			
35	865					870					875				880				
	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	Gly	Ile	Lys	Val	Asn			
				885					890						895				
	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	Val	Gln	Leu	Ala	Asp			
				900				905						910					
40	His	Tyr	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	Pro	Val	Leu	Leu	Pro				
		915					920					925							
	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	Ser	Lys	Asp	Pro	Asn			
		930					935					940							
	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	Val	Thr	Ala	Ala	Gly			
45	945					950					955				960				
	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys									
					965				970										

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(E) STRANDEDNESS: single

(F) TOPOLOGY: linear

55

150

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- 5 (A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...1785
 (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

10	ATG GGC AAC GCC GCC GCC GCC AAG AAG GGC AGC GAG CAG GAG AGC GTG	48
	Met Gly Asn Ala Ala Ala Ala Lys Lys Gly Ser Glu Gln Glu Ser Val	
	1 5 10 15	
15	AAA GAG TTC CTA GCC AAA GCC AAG GAA GAT TTC CTG AAA AAA TGG GAA	96
	Lys Glu Phe Leu Ala Lys Ala Lys Glu Asp Phe Leu Lys Lys Trp Glu	
	20 25 30	
20	GAC CCC TCT CAG AAT ACA GCC CAG TTG GAT CAG TTT GAT AGA ATC AAG	144
	Asp Pro Ser Gln Asn Thr Ala Gln Leu Asp Gln Phe Asp Arg Ile Lys	
	35 40 45	
25	ACC CTT GGC ACC GGC TCC TTT GGG CGA GTG ATG CTG GTG AAG CAC AAG	192
	Thr Leu Gly Thr Gly Ser Phe Gly Arg Val Met Leu Val Lys His Lys	
	50 55 60	
30	GAG AGT GGG AAC CAC TAC GCC ATG AAG ATC TTA GAC AAG CAG AAG GTG	240
	Glu Ser Gly Asn His Tyr Ala Met Lys Ile Leu Asp Lys Gln Lys Val	
	65 70 75 80	
35	GTG AAG CTA AAG CAG ATC GAG CAC ACT CTG AAT GAG AAG CGC ATC CTG	288
	Val Lys Leu Lys Gln Ile Glu His Thr Leu Asn Glu Lys Arg Ile Leu	
	85 90 95	
40	CAG GCC GTC AAC TTC CCG TTC CTG GTC AAA CTT GAA TTC TCC TTC AAG	336
	Gln Ala Val Asn Phe Pro Phe Leu Val Lys Leu Glu Phe Ser Phe Lys	
	100 105 110	
45	GAC AAC TCA AAC CTG TAC ATG GTC ATG GAG TAT GTA GCT GGT GGC GAG	384
	Asp Asn Ser Asn Leu Tyr Met Val Met Glu Tyr Val Ala Gly Gly Glu	
	115 120 125	
50	ATG TTC TCC CAC CTA CGG CGG ATT GGA AGG TTC AGC GAG CCC CAT GCC	432
	Met Phe Ser His Leu Arg Arg Ile Gly Arg Phe Ser Glu Pro His Ala	
	130 135 140	
55	CGT TTC TAC GCG GCG CAG ATC GTC CTG ACC TTT GAG TAT CTG CAC TCC	480
	Arg Phe Tyr Ala Ala Gln Ile Val Leu Thr Phe Glu Tyr Leu His Ser	
	145 150 155 160	
60	CAG CAG GCC TAT ATT CAG GTG ACA GAC TTC GGT TTT GCC AAG CGT GTG	576
	Gln Gln Gly Tyr Ile Gln Val Thr Asp Phe Gly Phe Ala Lys Arg Val	
	180 185 190	

151

5	AAA GGC CGT ACT TGG ACC TTG TGT GGG ACC CCT GAG TAC TTG GCC CCC	624
	Lys Gly Arg Thr Trp Thr Leu Cys Gly Thr Pro Glu Tyr Leu Ala Pro	
	195 200 205	
10	GAG ATT ATC CTG AGC AAA GGC TAC AAC AAG GCT GTG GAC TGG TGG GCT	672
	Glu Ile Ile Leu Ser Lys Gly Tyr Asn Lys Ala Val Asp Trp Trp Ala	
	210 215 220	
15	CTC GGA GTC CTC ATC TAC GAG ATG GCT GCT GGT TAC CCA CCC TTC TTC	720
	Leu Gly Val Leu Ile Tyr Glu Met Ala Ala Gly Tyr Pro Pro Phe Phe	
	225 230 235 240	
20	GCT GAC CAG CCT ATC CAG ATC TAT GAG AAA ATC GTC TCT GGG AAG GTG	768
	Ala Asp Gln Pro Ile Gln Ile Tyr Glu Lys Ile Val Ser Gly Lys Val	
	245 250 255	
25	CGG TTC CCA TCC CAC TTC AGC TCT GAC TTG AAG GAC CTG CTG CGG AAC	816
	Arg Phe Pro Ser His Phe Ser Ser Asp Leu Lys Asp Leu Leu Arg Asn	
	260 265 270	
30	CTT CTG CAA GTG GAT CTA ACC AAG CGC TTT GGA AAC CTC AAG GAC GGG	864
	Leu Leu Gln Val Asp Leu Thr Lys Arg Phe Gly Asn Leu Lys Asp Gly	
	275 280 285	
35	GTC AAT GAC ATC AAG AAC CAC AAG TGG TTT GCC ACG ACT GAC TGG ATT	912
	Val Asn Asp Ile Lys Asn His Lys Trp Phe Ala Thr Thr Asp Trp Ile	
	290 295 300	
40	GCC ATC TAT CAG AGA AAG GTG GAA GCT CCC TTC ATA CCA AAG TTT AAA	960
	Ala Ile Tyr Gln Arg Lys Val Glu Ala Pro Phe Ile Pro Lys Phe Lys	
	305 310 315 320	
45	GGC CCT GGG GAC ACG AGT AAC TTT GAC GAC TAT GAG GAG GAA GAG ATC	1008
	Gly Pro Gly Asp Thr Ser Asn Phe Asp Asp Tyr Glu Glu Glu Glu Ile	
	325 330 335	
50	CGG GTC TCC ATC AAT GAG AAG TGT GGC AAG GAG TTT ACT GAG TTT GGG	1056
	Arg Val Ser Ile Asn Glu Lys Cys Gly Lys Glu Phe Thr Glu Phe Gly	
	340 345 350	
55	CGC GCC ATG AGT AAA GGA GAA GAA CTT TTC ACT GGA GTT GTC CCA ATT	1104
	Arg Ala Met Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile	
	355 360 365	
60	CTT GTT GAA TTA GAT GGC GAT GTT AAT GGG CAA AAA TTC TCT GTT AGT	1152
	Leu Val Glu Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val Ser	
	370 375 380	
65	ATT TGC ACT ACT GGG AAG CTA CCT GTT CCA TGG CCA ACG CTT GTC ACT	1248
	Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr	
	405 410 415	

152

	ACT CTC ACT TAT GGT GTT CAA TGC TTT TCT AGA TAC CCA GAT CAT ATG	1296
	Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met	
	420 425 430	
5	AAA CAG CAT GAC TTT TTC AAG AGT GCC ATG CCC GAA GGT TAT GTA CAG	1344
	Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln	
	435 440 445	
10	GAA AGA ACT ATA TTT TAC AAA GAT GAC GGG AAC TAC AAG ACA CGT GCT	1392
	Glu Arg Thr Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala	
	450 455 460	
15	GAA GTC AAG TTT GAA GGT GAT ACC CTT GTT AAT AGA ATC GAG TTA AAA	1440
	Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys	
	465 470 475 480	
20	GGT ATT GAT TTT AAA GAA GAT GGA AAC ATT CTT GGA CAC AAA ATG GAA	1488
	Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met Glu	
	485 490 495	
25	TAC AAT TAT AAC TCA CAT AAT GTA TAC ATC ATG GCA GAC AAA CCA AAG	1536
	Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro Lys	
	500 505 510	
30	AAT GGC ATC AAA GTT AAC TTC AAA ATT AGA CAC AAC ATT AAA GAT GGA	1584
	Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp Gly	
	515 520 525	
35	AGC GTT CAA TTA GCA GAC CAT TAT CAA CAA AAT ACT CCA ATT GGC GAT	1632
	Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp	
	530 535 540	
40	GGC CCT GTC CTT TTA CCA GAC AAC CAT TAC CTG TCC ACG CAA TCT GCC	1680
	Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala	
	545 550 555 560	
45	CTT TCC AAA GAT CCC AAC GAA AAG AGA GAT CAC ATG ATC CTT CTT GAG	1728
	Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu Glu	
	565 570 575	
50	TTT GTA ACA GCT GCT GGG ATT ACA CAT GGC ATG GAT GAA CTA TAC AAA	1776
	Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys	
	580 585 590	
55	CCT CAG GAG TAA	1788
	Pro Gln Glu	
	595	

SEQUENCE CHARACTERISTICS

- (A) LENGTH: 595 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single

154

385 390 395 400
 Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr
 405 410 415
 5 Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met
 420 425 430
 Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln
 435 440 445
 Glu Arg Thr Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala
 450 455 460
 10 Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys
 465 470 475 480
 Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met Glu
 485 490 495
 15 Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro Lys
 500 505 510
 Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp Gly
 515 520 525
 Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp
 530 535 540
 20 Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala
 545 550 555 560
 Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu Glu
 565 570 575
 25 Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys
 580 585 590
 Pro Gln Glu
 595

(2) INFORMATION FOR SEQ ID NO:70:

30

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2181 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 35 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

40

- (A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...2178
 (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

45

ATG AGC GAC GTG GCT ATT GTG AAG GAG GGT TGG CTG CAC AAA CGA GGG 48
 Met Ser Asp Val Ala Ile Val Lys Glu Gly Trp Leu His Lys Arg Gly
 1 5 10

55

GGC ACC TTC ATT GGC TAC AAG GAG CGG CCG CAG GAT GTG GAC CAA CGT 144
 Gly Thr Phe Ile Gly Tyr Lys Glu Arg Pro Gln Asp Val Asp Gln Arg
 35 40

155

	GAG GCT CCC CTC AAC AAC TTC TCT GTG GCG CAG TGC CAG CTG ATG AAG	192
	Glu Ala Pro Leu Asn Asn Phe Ser Val Ala Gln Cys Gln Leu Met Lys	
	50 55 60	
5	ACG GAG CGG CCC CGG CCC AAC ACC TTC ATC ATC CGC TGC CTG CAG TGG	240
	Thr Glu Arg Pro Arg Pro Asn Thr Phe Ile Ile Arg Cys Leu Gln Trp	
	65 70 75 80	
10	ACC ACT GTC ATC GAA CGC ACC TTC CAT GTG GAG ACT CCT GAG GAG CGG	288
	Thr Thr Val Ile Glu Arg Thr Phe His Val Glu Thr Pro Glu Glu Arg	
	85 90 95	
15	GAG GAG TGG ACA ACC GCC ATC CAG ACT GTG GCT GAC GGC CTC AAG AAG	336
	Glu Glu Trp Thr Thr Ala Ile Gln Thr Val Ala Asp Gly Leu Lys Lys	
	100 105 110	
20	CAG GAG GAG GAG GAG ATG GAC TTC CGG TCG GGC TCA CCC AGT GAC AAC	384
	Gln Glu Glu Glu Glu Met Asp Phe Arg Ser Gly Ser Pro Ser Asp Asn	
	115 120 125	
25	TCA GGG GCT GAA GAG ATG GAG GTG TCC CTG GCC AAG CCC AAG CAC CGC	432
	Ser Gly Ala Glu Glu Met Glu Val Ser Leu Ala Lys Pro Lys His Arg	
	130 135 140	
30	GTG ACC ATG AAC GAG TTT GAG TAC CTG AAG CTG CTG GGC AAG GGC ACT	480
	Val Thr Met Asn Glu Phe Glu Tyr Leu Lys Leu Leu Gly Lys Gly Thr	
	145 150 155 160	
35	TTC GGC AAG GTG ATC CTG GTG AAG GAG AAG GCC ACA GGC CGC TAC TAC	528
	Phe Gly Lys Val Ile Leu Val Lys Glu Lys Ala Thr Gly Arg Tyr Tyr	
	165 170 175	
40	GCC ATG AAG ATC CTC AAG AAG GAA GTC ATC GTG GCC AAG GAC GAG GTG	576
	Ala Met Lys Ile Leu Lys Lys Glu Val Ile Val Ala Lys Asp Glu Val	
	180 185 190	
45	GCC CAC ACA CTC ACC GAG AAC CGC GTC CTG CAG AAC TCC AGG CAC CCC	624
	Ala His Thr Leu Thr Glu Asn Arg Val Leu Gln Asn Ser Arg His Pro	
	195 200 205	
50	TTC CTC ACA GCC CTG AAG TAC TCT TTC CAG ACC CAC GAC CGC CTC TGC	672
	Phe Leu Thr Ala Leu Lys Tyr Ser Phe Gln Thr His Asp Arg Leu Cys	
	210 215 220	
55	TTT GTC ATG GAG TAC GCC AAC GGG GGC GAG CTG TTC TTC CAC CTG TCC	720
	Phe Val Met Glu Tyr Ala Asn Gly Gly Glu Leu Phe Phe His Leu Ser	
	225 230 235 240	
60	ATT GTG TCA GCC CTG GAC TAC CTG CAC TCG GAG AAG AAC GTG GTG TAC	816
	Ile Val Ser Ala Leu Asp Tyr Leu His Ser Glu Lys Asn Val Val Tyr	
	260 265 270	

156

	CGG GAC CTC AAG CTG GAG AAC CTC ATG CTG GAC AAG GAC GGG CAC ATT	864
	Arg Asp Leu Lys Leu Glu Asn Leu Met Leu Asp Lys Asp Gly His Ile	
	275 280 285	
5	AAG ATC ACA GAC TTC GGG CTG TGC AAG GAG GGG ATC AAG GAC GGT GCC	912
	Lys Ile Thr Asp Phe Gly Leu Cys Lys Glu Gly Ile Lys Asp Gly Ala	
	290 295 300	
10	ACC ATG AAG ACC TTT TGC GGC ACA CCT GAG TAC CTG GCC CCC GAG GTG	960
	Thr Met Lys Thr Phe Cys Gly Thr Pro Glu Tyr Leu Ala Pro Glu Val	
	305 310 315 320	
15	CTG GAG GAC AAT GAC TAC GGC CGT GCA GTG GAC TGG TGG GGG CTG GGC	1008
	Leu Glu Asp Asn Asp Tyr Gly Arg Ala Val Asp Trp Trp Gly Leu Gly	
	325 330 335	
20	GTG GTC ATG TAC GAG ATG ATG TGC GGT CGC CTG CCC TTC TAC AAC CAG	1056
	Val Val Met Tyr Glu Met Met Cys Gly Arg Leu Pro Phe Tyr Asn Gln	
	340 345 350	
25	GAC CAT GAG AAG CTT TTT GAG CTC ATC CTC ATG GAG GAG ATC CGC TTC	1104
	Asp His Glu Lys Leu Phe Glu Leu Ile Leu Met Glu Glu Ile Arg Phe	
	355 360 365	
30	CCG CGC ACG CTT GGT CCC GAG GCC AAG TCC TTG CTT TCA GGG CTG CTC	1152
	Pro Arg Thr Leu Gly Pro Glu Ala Lys Ser Leu Leu Ser Gly Leu Leu	
	370 375 380	
35	AAG AAG GAC CCC AAG CAG AGG CTT GGC GGG GGC TCC GAG GAC GCC AAG	1200
	Lys Lys Asp Pro Lys Gln Arg Leu Gly Gly Gly Ser Glu Asp Ala Lys	
	385 390 395 400	
40	GAG ATC ATG CAG CAT CGC TTC TTT GCC GGT ATC GTG TGG CAG CAC GTG	1248
	Glu Ile Met Gln His Arg Phe Phe Ala Gly Ile Val Trp Gln His Val	
	405 410 415	
45	TAC GAG AAG AAG CTC AGC CCA CCC TTC AAG CCC CAG GTC ACG TCG GAG	1296
	Tyr Glu Lys Lys Leu Ser Pro Pro Phe Lys Pro Gln Val Thr Ser Glu	
	420 425 430	
50	ACT GAC ACC AGG TAT TTT GAT GAG GAG TTC ACG GCC CAG ATG ATC ACC	1344
	Thr Asp Thr Arg Tyr Phe Asp Glu Glu Phe Thr Ala Gln Met Ile Thr	
	435 440 445	
55	ATC ACA CCA CCT GAC CAA GAT GAC AGC ATG GAG TGT GTG GAC AGC GAG	1392
	Ile Thr Pro Pro Asp Gln Asp Ser Met Glu Cys Val Asp Ser Glu	
	450 455 460	
60	TGG GAT CCA CCG GTC GGC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC	1488
	Ser Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe	
	485 490 495	

157

	ACC GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC	1536
	Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly	
	500 505 510	
5	CAC AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC	1584
	His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly	
	515 520 525	
10	AAG CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC	1632
	Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro	
	530 535 540	
15	TGG CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC	1680
	Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser	
	545 550 555 560	
20	CGC TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG	1728
	Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met	
	565 570 575	
25	CCC GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC	1776
	Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly	
	580 585 590	
30	AAC TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG	1824
	Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val	
	595 600 605	
35	AAC CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC	1872
	Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile	
	610 615 620	
40	CTG GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC	1920
	Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile	
	625 630 635 640	
45	ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC	1968
	Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg	
	645 650 655	
50	CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG	2016
	His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln	
	660 665 670	
55	AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC	2064
	Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr	
	675 680 685	
60	CAC ATG GTC CTC CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC	2160
	His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly	
	705 710 715 720	

158

ATG GAC GAG CTG TAC AAG TAA
Met Asp Glu Leu Tyr Lys
725

2181

5

(2) INFORMATION FOR SEQ ID NO:71:

- (i) SEQUENCE CHARACTERISTICS:
10 (A) LENGTH: 726 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- 15 (ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO.71:

20 Met Ser Asp Val Ala Ile Val Lys Glu Gly Trp Leu His Lys Arg Gly
1 5 10 15
Glu Tyr Ile Lys Thr Trp Arg Pro Arg Tyr Phe Leu Leu Lys Asn Asp
20 25 30
25 Gly Thr Phe Ile Gly Tyr Lys Glu Arg Pro Gln Asp Val Asp Gln Arg
35 40 45
Glu Ala Pro Leu Asn Asn Phe Ser Val Ala Gln Cys Gln Leu Met Lys
50 55 60
Thr Glu Arg Pro Arg Pro Asn Thr Phe Ile Ile Arg Cys Leu Gln Trp
65 70 75 80
30 Thr Thr Val Ile Glu Arg Thr Phe His Val Glu Thr Pro Glu Glu Arg
85 90 95
Glu Glu Trp Thr Thr Ala Ile Gln Thr Val Ala Asp Gly Leu Lys Lys
100 105 110
Gln Glu Glu Glu Glu Met Asp Phe Arg Ser Gly Ser Pro Ser Asp Asn
35 115 120 125
Ser Gly Ala Glu Glu Met Glu Val Ser Leu Ala Lys Pro Lys His Arg
130 135 140
Val Thr Met Asn Glu Phe Glu Tyr Leu Lys Leu Leu Gly Lys Gly Thr
145 150 155 160
40 Phe Gly Lys Val Ile Leu Val Lys Glu Lys Ala Thr Gly Arg Tyr Tyr
165 170 175
Ala Met Lys Ile Leu Lys Lys Glu Val Ile Val Ala Lys Asp Glu Val
180 185 190
Ala His Thr Leu Thr Glu Asn Arg Val Leu Gln Asn Ser Arg His Pro
45 195 200 205
Phe Leu Thr Ala Leu Lys Tyr Ser Phe Gln Thr His Asp Arg Leu Cys
210 215 220
Phe Val Met Glu Tyr Ala Asn Gly Gly Glu Leu Phe Phe His Leu Ser
225 230
235 240
245 250
255 260
265 270
55 Arg Asp Leu Lys Leu Glu Asn Leu Met Leu Asp Lys Asp Gly His Ile
275 280 285
Lys Ile Thr Asp Phe Gly Leu Cys Lys Glu Gly Ile Lys Asn Glu Ala

[illegible]

160

(2) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 2751 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

10 (ix) FEATURE:

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...2748

(D) OTHER INFORMATION:

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

20	ATG GCT GAC GTT TAC CCG GCC AAC GAC TCC ACG GCG TCT CAG GAC GTG	48
	Met Ala Asp Val Tyr Pro Ala Asn Asp Ser Thr Ala Ser Gln Asp Val	
	1 5 10 15	
	GCC AAC CGC TTC GCC CGC AAA GGG GCG CTG AGG CAG AAG AAC GTG CAT	96
	Ala Asn Arg Phe Ala Arg Lys Gly Ala Leu Arg Gln Lys Asn Val His	
	20 25 30	
25	GAG GTG AAA GAC CAC AAA TTC ATC GCC CGC TTC TTC AAG CAA CCC ACC	144
	Glu Val Lys Asp His Lys Phe Ile Ala Arg Phe Phe Lys Gln Pro Thr	
	35 40 45	
30	TTC TGC AGC CAC TGC ACC GAC TTC ATC TGG GGG TTT GGG AAA CAA GGC	192
	Phe Cys Ser His Cys Thr Asp Phe Ile Trp Gly Phe Gly Lys Gln Gly	
	50 55 60	
35	TTC CAG TGC CAA GTT TGC TGT TTT GTG GTT CAT AAG AGG TGC CAT GAG	240
	Phe Gln Cys Gln Val Cys Cys Phe Val Val His Lys Arg Cys His Glu	
	65 70 75 80	
	TTC GTT ACG TTC TCT TGT CCG GGT GCG GAT AAG GGA CCT GAC ACT GAC	288
	Phe Val Thr Phe Ser Cys Pro Gly Ala Asp Lys Gly Pro Asp Thr Asp	
40	85 90 95	
	GAC CCC AGG AGC AAG CAC AAG TTC AAA ATC CAC ACA TAC GGA AGC CCT	336
	Asp Pro Arg Ser Lys His Lys Phe Lys Ile His Thr Tyr Gly Ser Pro	
	100 105 110	
45	ACC TTC TGT GAT CAC TGT GGG TCC CTG CTC TAT GGA CTT ATC CAC CAA	384
	Thr Phe Cys Asp His Cys Gly Ser Leu Leu Tyr Gly Leu Ile His Gln	
	115 120 125	
55	ATC AAT GAC CCT AGC CTC TGC GGA ATG GAT CAC ACA GAG AAG AGG GGG	480
	Ile Asn Asp Pro Ser Leu Cys Gly Met Asp His Thr Glu Lys Arg Gly	
	145 150 155	

161

	CGG ATT TAT CTG AAG GCT GAG GTC ACT GAT GAA AAG CTC CAC GTC ACG	528
	Arg Ile Tyr Leu Lys Ala Glu Val Thr Asp Glu Lys Leu His Val Thr	
	165 170 175	
5	GTA CGA GAT GCA AAA AAT CTA ATC CCT ATG GAT CCA AAT GGG CTT TCG	576
	Val Arg Asp Ala Lys Asn Leu Ile Pro Met Asp Pro Asn Gly Leu Ser	
	180 185 190	
10	GAT CCT TAT GTG AAG CTG AAA CTA ATC CCT GAC CCC AAG AAT GAG AGC	624
	Asp Pro Tyr Val Lys Leu Lys Leu Ile Pro Asp Pro Lys Asn Glu Ser	
	195 200 205	
15	AAA CAG AAA ACC AAA ACC ATC CGC TCC AAC CTG AAT CCT CAG TGG AAT	672
	Lys Gln Lys Thr Lys Thr Ile Arg Ser Asn Leu Asn Pro Gln Trp Asn	
	210 215 220	
20	GAG TCC TTC ACG TTC AAA TTA AAA CCT TCA GAC AAA GAC CGG CGA CTG	720
	Glu Ser Phe Thr Phe Lys Leu Lys Pro Ser Asp Lys Asp Arg Arg Leu	
	225 230 235 240	
25	TCT GTA GAA ATC TGG GAC TGG GAT CGG ACG ACT CGG AAT GAC TTC ATG	768
	Ser Val Glu Ile Trp Asp Trp Asp Arg Thr Thr Arg Asn Asp Phe Met	
	245 250 255	
30	GGA TCC CTT TCC TTT GGT GTC TCA GAG CTA ATG AAG ATG CCG GCC AGT	816
	Gly Ser Leu Ser Phe Gly Val Ser Glu Leu Met Lys Met Pro Ala Ser	
	260 265 270	
35	GGA TGG TAT AAA GCT CAC AAC CAA GAA GAG GGC GAA TAT TAC AAC GTG	864
	Gly Trp Tyr Lys Ala His Asn Gln Glu Glu Gly Glu Tyr Tyr Asn Val	
	275 280 285	
40	CCC ATT CCA GAA GGA GAT GAA GAA GGC AAC ATG GAA CTC AGG CAG AAG	912
	Pro Ile Pro Glu Gly Asp Glu Glu Gly Asn Met Glu Leu Arg Gln Lys	
	290 295 300	
45	TTT GAG AAA GCC AAG CTA GGT CCT GTT GGT AAC AAA GTC ATC AGC CCT	960
	Phe Glu Lys Ala Lys Leu Gly Pro Val Gly Asn Lys Val Ile Ser Pro	
	305 310 315 320	
50	TCA GAA GAC AGA AAG CAA CCA TCC AAC AAC CTG GAC AGA GTG AAA CTC	1008
	Ser Glu Asp Arg Lys Gln Pro Ser Asn Asn Leu Asp Arg Val Lys Leu	
	325 330 335	
55	ACA GAC TTC AAC TTC CTC ATG GTG CTG GGG AAG GGG AGT TTT GGG AAG	1056
	Thr Asp Phe Asn Phe Leu Met Val Leu Gly Lys Gly Ser Phe Gly Lys	
	340 345 350	
60	ATC CTG AAG AAG GAC GTG GTG ATC CAG GAC GAC GAC GTG GAG TGC ACC	1152
	Ile Leu Lys Lys Asp Val Val Ile Gln Asp Asp Asp Val Glu Cys Thr	
	370 375 380	

162

5	ATG GTG GAG AAG CGC GTG CTG GCC CTG CTG GAC AAG CCG CCA TTT CTG	1200
	Met Val Glu Lys Arg Val Leu Ala Leu Leu Asp Lys Pro Pro Phe Leu	
	385 390 395 400	
10	ACA CAG CTG CAC TCC TGC TTC CAG ACA GTG GAC CGG CTG TAC TTC GTC	1248
	Thr Gln Leu His Ser Cys Phe Gln Thr Val Asp Arg Leu Tyr Phe Val	
	405 410 415	
15	ATG GAA TAC GTC AAC GGC GGG GAT CTT ATG TAC CAC ATT CAG CAA GTC	1296
	Met Glu Tyr Val Asn Gly Gly Asp Leu Met Tyr His Ile Gln Gln Val	
	420 425 430	
20	GGG AAA TTT AAG GAG CCA CAA GCA GTA TTC TAC GCA GCC GAG ATC TCC	1344
	Gly Lys Phe Lys Glu Pro Gln Ala Val Phe Tyr Ala Ala Glu Ile Ser	
	435 440 445	
25	ATC GGA CTG TTC TTC CTT CAT AAA AGA GGG ATC ATT TAC AGG GAT CTG	1392
	Ile Gly Leu Phe Phe Leu His Lys Arg Gly Ile Ile Tyr Arg Asp Leu	
	450 455 460	
30	AAG CTG AAC AAT GTC ATG CTG AAC TCA GAA GGG CAC ATC AAA ATC GCC	1440
	Lys Leu Asn Asn Val Met Leu Asn Ser Glu Gly His Ile Lys Ile Ala	
	465 470 475 480	
35	GAC TTC GGG ATG TGC AAG GAA CAC ATG ATG GAT GGA GTC ACG ACC AGG	1488
	Asp Phe Gly Met Cys Lys Glu His Met Met Asp Gly Val Thr Thr Arg	
	485 490 495	
40	ACC TTC TGC GGA ACT CCG GAC TAC ATT GCC CCA GAG ATA ATC GCT TAC	1536
	Thr Phe Cys Gly Thr Pro Asp Tyr Ile Ala Pro Glu Ile Ile Ala Tyr	
	500 505 510	
45	CAG CCG TAC GGG AAG TCT GTA GAT TGG TGG GCG TAC GGT GTG CTG CTG	1584
	Gln Pro Tyr Gly Lys Ser Val Asp Trp Trp Ala Tyr Gly Val Leu Leu	
	515 520 525	
50	TAC GAG ATG CTA GCC GGG CAG CCT CCG TTT GAT GGT GAA GAT GAA GAT	1632
	Tyr Glu Met Leu Ala Gly Gln Pro Pro Phe Asp Gly Glu Asp Glu Asp	
	530 535 540	
55	GAA CTG TTT CAG TCT ATA ATG GAG CAC AAC GTG TCC TAC CCC AAA TCC	1680
	Glu Leu Phe Gln Ser Ile Met Glu His Asn Val Ser Tyr Pro Lys Ser	
	545 550 555 560	
60	TTG TCC AAG GAA GCC GTC TCC ATC TGC AAA GGA CTT ATG ACC AAA CAG	1728
	Leu Ser Lys Glu Ala Val Ser Ile Cys Lys Gly Leu Met Thr Lys Gln	
	565 570 575	
65	GAG CAT GCC TTC TTC AGG AGG ATC GAC TGG GAG AAA CTG GAG AAC AGG	1824
	Glu His Ala Phe Phe Arg Arg Ile Asp Trp Glu Lys Leu Glu Asn Arg	
	595 600 605	

163

	GAG	ATC	CAA	CCA	CCA	TTC	AAG	CCC	AAA	GTG	TGT	GGC	AAA	GGA	GCA	GAA	1872
	Glu	Ile	Gln	Pro	Pro	Phe	Lys	Pro	Lys	Val	Cys	Gly	Lys	Gly	Ala	Glu	
		610					615					620					
5	AAC	TTT	GAC	AAG	TTC	TTC	ACG	CGA	GGA	CAG	CCT	GTC	TTA	ACA	CCA	CCA	1920
	Asn	Phe	Asp	Lys	Phe	Phe	Thr	Arg	Gly	Gln	Pro	Val	Leu	Thr	Pro	Pro	
	625					630					635					640	
10	GAT	CAG	CTG	GTC	ATT	GCT	AAC	ATA	GAC	CAA	TCT	GAT	TTT	GAA	GGG	TTC	1968
	Asp	Gln	Leu	Val	Ile	Ala	Asn	Ile	Asp	Gln	Ser	Asp	Phe	Glu	Gly	Phe	
					645					650					655		
15	TCG	TAT	GTC	AAC	CCC	CAG	TTT	GTG	CAC	CCA	ATC	TTG	CAA	AGT	GCA	GTA	2016
	Ser	Tyr	Val	Asn	Pro	Gln	Phe	Val	His	Pro	Ile	Leu	Gln	Ser	Ala	Val	
				660					665						670		
20	GGG	CGC	GCC	ATG	AGT	AAA	GGA	GAA	GAA	CTT	TTC	ACT	GGA	GTT	GTC	CCA	2064
	Gly	Arg	Ala	Met	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	
			675					680					685				
25	ATT	CTT	GTT	GAA	TTA	GAT	GGC	GAT	GTT	AAT	GGG	CAA	AAA	TTC	TCT	GTT	2112
	Ile	Leu	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	Gln	Lys	Phe	Ser	Val	
		690					695					700					
30	AGT	GGA	GAG	GGT	GAA	GGT	GAT	GCA	ACA	TAC	GGA	AAA	CTT	ACC	CTT	AAA	2160
	Ser	Gly	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	
	705					710					715					720	
35	TTT	ATT	TGC	ACT	ACT	GGG	AAG	CTA	CCT	GTT	CCA	TGG	CCA	ACG	CTT	GTC	2208
	Phe	Ile	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	
					725					730					735		
40	ACT	ACT	CTC	ACT	TAT	GGT	GTT	CAA	TGC	TTT	TCT	AGA	TAC	CCA	GAT	CAT	2256
	Thr	Thr	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	
				740					745					750			
45	ATG	AAA	CAG	CAT	GAC	TTT	TTC	AAG	AGT	GCC	ATG	CCC	GAA	GGT	TAT	GTA	2304
	Met	Lys	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	
			755					760					765				
50	CAG	GAA	AGA	ACT	ATA	TTT	TAC	AAA	GAT	GAC	GGG	AAC	TAC	AAG	ACA	CGT	2352
	Gln	Glu	Arg	Thr	Ile	Phe	Tyr	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	
		770					775					780					
55	GCT	GAA	GTC	AAG	TTT	GAA	GGT	GAT	ACC	CTT	GTT	AAT	AGA	ATC	GAG	TTA	2400
	Ala	Glu	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	
	785					790					795						
60	GAA	TAC	AAT	TAT	AAC	TCA	CAT	AAT	GTA	TAC	ATC	ATG	GCA	GAC	AAA	CCA	2496
	Glu	Tyr	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Pro	
				820					825								

164

AAG AAT GGC ATC AAA GTT AAC TTC AAA ATT AGA CAC AAC ATT AAA GAT 2544
 Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp
 835 840 845
 5
 GGA AGC GTT CAA TTA GCA GAC CAT TAT CAA CAA AAT ACT CCA ATT GGC 2592
 Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly
 850 855 860
 10
 GAT GGC CCT GTC CTT TTA CCA GAC AAC CAT TAC CTG TCC ACG CAA TCT 2640
 Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser
 865 870 875 880
 15
 GCC CTT TCC AAA GAT CCC AAC GAA AAG AGA GAT CAC ATG ATC CTT CTT 2688
 Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu
 885 890 895
 20
 GAG TTT GTA ACA GCT GCT GGG ATT ACA CAT GGC ATG GAT GAA CTA TAC 2736
 Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr
 900 905 910
 AAA CCT CAG GAG TAA 2751
 Lys Pro Gln Glu
 915
 25

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:
 30 (A) LENGTH: 916 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 35 (ii) MOLECULE TYPE: protein
 (v) FRAGMENT TYPE: internal
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:
 40 Met Ala Asp Val Tyr Pro Ala Asn Asp Ser Thr Ala Ser Gln Asp Val
 1 5 10 15
 Ala Asn Arg Phe Ala Arg Lys Gly Ala Leu Arg Gln Lys Asn Val His
 20 25 30
 45 Glu Val Lys Asp His Lys Phe Ile Ala Arg Phe Phe Lys Gln Pro Thr
 35 40 45
 Phe Cys Ser His Cys Thr Asp Phe Ile Trp Gly Phe Gly Lys Gln Gly
 50 55 60
 Phe Gln Cys Gln Val Cys Cys Phe Val Val His Leu Leu Gln Val
 65 70 75 80 85
 100 105 110
 55 Thr Phe Cys Asp His Cys Gly Ser Leu Leu Tyr Gly Leu Ile His Gln
 115 120 125
 Gly Met Lys Cys Asp Thr Cys Asp Met Asp Val Thr Asp Val Thr

	Ile	Asn	Asp	Pro	Ser	Leu	Cys	Gly	Met	Asp	His	Thr	Glu	Lys	Arg	Gly	
	145					150					155					160	
5	Arg	Ile	Tyr	Leu	Lys	Ala	Glu	Val	Thr	Asp	Glu	Lys	Leu	His	Val	Thr	
					165					170					175		
	Val	Arg	Asp	Ala	Lys	Asn	Leu	Ile	Pro	Met	Asp	Pro	Asn	Gly	Leu	Ser	
				180					185					190			
	Asp	Pro	Tyr	Val	Lys	Leu	Lys	Leu	Ile	Pro	Asp	Pro	Lys	Asn	Glu	Ser	
			195					200					205				
10	Lys	Gln	Lys	Thr	Lys	Thr	Ile	Arg	Ser	Asn	Leu	Asn	Pro	Gln	Trp	Asn	
	210						215					220					
	Glu	Ser	Phe	Thr	Phe	Lys	Leu	Lys	Pro	Ser	Asp	Lys	Asp	Arg	Arg	Leu	
	225					230					235					240	
15	Ser	Val	Glu	Ile	Trp	Asp	Trp	Asp	Arg	Thr	Thr	Arg	Asn	Asp	Phe	Met	
				245						250					255		
	Gly	Ser	Leu	Ser	Phe	Gly	Val	Ser	Glu	Leu	Met	Lys	Met	Pro	Ala	Ser	
				260					265					270			
	Gly	Trp	Tyr	Lys	Ala	His	Asn	Gln	Glu	Glu	Gly	Glu	Tyr	Asn	Val		
	275						280						285				
20	Pro	Ile	Pro	Glu	Gly	Asp	Glu	Glu	Gly	Asn	Met	Glu	Leu	Arg	Gln	Lys	
	290						295					300					
	Phe	Glu	Lys	Ala	Lys	Leu	Gly	Pro	Val	Gly	Asn	Lys	Val	Ile	Ser	Pro	
	305					310					315					320	
25	Ser	Glu	Asp	Arg	Lys	Gln	Pro	Ser	Asn	Asn	Leu	Asp	Arg	Val	Lys	Leu	
				325						330					335		
	Thr	Asp	Phe	Asn	Phe	Leu	Met	Val	Leu	Gly	Lys	Gly	Ser	Phe	Gly	Lys	
				340					345						350		
	Val	Met	Leu	Ala	Asp	Arg	Lys	Gly	Thr	Glu	Glu	Leu	Tyr	Ala	Ile	Lys	
	355						360					365					
30	Ile	Leu	Lys	Lys	Asp	Val	Val	Ile	Gln	Asp	Asp	Asp	Val	Glu	Cys	Thr	
	370						375					380					
	Met	Val	Glu	Lys	Arg	Val	Leu	Ala	Leu	Leu	Asp	Lys	Pro	Pro	Phe	Leu	
	385					390					395					400	
35	Thr	Gln	Leu	His	Ser	Cys	Phe	Gln	Thr	Val	Asp	Arg	Leu	Tyr	Phe	Val	
				405						410					415		
	Met	Glu	Tyr	Val	Asn	Gly	Gly	Asp	Leu	Met	Tyr	His	Ile	Gln	Gln	Val	
				420					425					430			
	Gly	Lys	Phe	Lys	Glu	Pro	Gln	Ala	Val	Phe	Tyr	Ala	Ala	Glu	Ile	Ser	
	435						440						445				
40	Ile	Gly	Leu	Phe	Phe	Leu	His	Lys	Arg	Gly	Ile	Ile	Tyr	Arg	Asp	Leu	
	450																

166

					580					585				590					
		Glu	His	Ala	Phe	Phe	Arg	Arg	Ile	Asp	Trp	Glu	Lys	Leu	Glu	Asn	Arg		
				595					600					605					
5		Glu	Ile	Gln	Pro	Pro	Phe	Lys	Pro	Lys	Val	Cys	Gly	Lys	Gly	Ala	Glu		
		610						615					620						
		Asn	Phe	Asp	Lys	Phe	Phe	Thr	Arg	Gly	Gln	Pro	Val	Leu	Thr	Pro	Pro		
		625						630				635					640		
		Asp	Gln	Leu	Val	Ile	Ala	Asn	Ile	Asp	Gln	Ser	Asp	Phe	Glu	Gly	Phe		
						645					650					655			
10		Ser	Tyr	Val	Asn	Pro	Gln	Phe	Val	His	Pro	Ile	Leu	Gln	Ser	Ala	Val		
					660					665						670			
		Gly	Arg	Ala	Met	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro		
				675					680					685					
		Ile	Leu	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	Gln	Lys	Phe	Ser	Val		
		690						695					700						
		Ser	Gly	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys		
		705						710				715					720		
		Phe	Ile	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val		
						725					730					735			
20		Thr	Thr	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His		
					740					745					750				
		Met	Lys	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val		
				755					760					765					
		Gln	Glu	Arg	Thr	Ile	Phe	Tyr	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg		
		770						775					780						
25		Ala	Glu	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu		
		785					790					795				800			
		Lys	Gly	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Met		
					805						810					815			
30		Glu	Tyr	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Pro		
				820						825					830				
		Lys	Asn	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Lys	Asp		
				835					840					845					
		Gly	Ser	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly		
		850						855					860						
35		Asp	Gly	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser		
		865																	

45 (2) INFORMATION FOR SEO ID NO:74:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2157 base pairs

MOLECULE TYPE: cDNA

(ix) FEATURE:

55

(A) NAME/KEY: Coding Sequence

167

(B) LOCATION: 1...2154

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

5	ATG TCG TCC ATC TTG CCA TTC ACG CCG CCA GTT GTG AAG AGA CTG CTG	48
	Met Ser Ser Ile Leu Pro Phe Thr Pro Pro Val Val Lys Arg Leu Leu	
	1 5 10 15	
10	GGA TGG AAG AAG TCA GCT GGT GGG TCT GGA GGA GCA GGC GGA GGA GAG	96
	Gly Trp Lys Lys Ser Ala Gly Gly Ser Gly Gly Ala Gly Gly Gly Glu	
	20 25 30	
15	CAG AAT GGG CAG GAA CAA AAG TGG TGT GAG AAA GCA GTG AAA AGT CTG	144
	Gln Asn Gly Gln Glu Glu Lys Trp Cys Glu Lys Ala Val Lys Ser Leu	
	35 40 45	
20	GTG AAG AAG CTA AAG AAA ACA GGA CGA TTA GAT GAG CTT GAG AAA GCC	192
	Val Lys Lys Leu Lys Lys Thr Gly Arg Leu Asp Glu Leu Glu Lys Ala	
	50 55 60	
25	ATC ACC ACT CAA AAC TGT AAT ACT AAA TGT GTT ACC ATA CCA AGC ACT	240
	Ile Thr Thr Gln Asn Cys Asn Thr Lys Cys Val Thr Ile Pro Ser Thr	
	65 70 75 80	
30	TGC TCT GAA ATT TGG GGA CTG AGT ACA CCA AAT ACG ATA GAT CAG TGG	288
	Cys Ser Glu Ile Trp Gly Leu Ser Thr Pro Asn Thr Ile Asp Gln Trp	
	85 90 95	
35	GAT ACA ACA GGC CTT TAC AGC TTC TCT GAA CAA ACC AGG TCT CTT GAT	336
	Asp Thr Thr Gly Leu Tyr Ser Phe Ser Glu Gln Thr Arg Ser Leu Asp	
	100 105 110	
40	GGT CGT CTC CAG GTA TCC CAT CGA AAA GGA TTG CCA CAT GTT ATA TAT	384
	Gly Arg Leu Gln Val Ser His Arg Lys Gly Leu Pro His Val Ile Tyr	
	115 120 125	
45	TGC CGA TTA TGG CGC TGG CCT GAT CTT CAC AGT CAT CAT GAA CTC AAG	432
	Cys Arg Leu Trp Arg Trp Pro Asp Leu His Ser His His Glu Leu Lys	
	130 135 140	
50	GCA ATT GAA AAC TGC GAA TAT GCT TTT AAT CTT AAA AAG GAT GAA GTA	480
	Ala Ile Glu Asn Cys Glu Tyr Ala Phe Asn Leu Lys Lys Asp Glu Val	
	145 150 155 160	
55	TGT GTA AAC CCT TAC CAC TAT CAG AGA GTT GAG ACA CCA GTT TTG CCT	528
	Cys Val Asn Pro Tyr His Tyr Gln Arg Val Glu Thr Pro Val Leu Pro	
	165 170 175	
60	CTG GAT GAC TAT ACT CAC TCC ATT CCA GAA AAC ACT AAC TTC CCA GCA	624
	Leu Asp Asp Tyr Thr His Ser Ile Pro Glu Asn Thr Asn Phe Pro Ala	
	180 185 190 195 200	

168

5	GGA	ATT	GAG	CCA	CAG	AGT	AAT	TAT	ATT	CCA	GAA	ACG	CCA	CCT	CCT	GGA	672
	Gly	Ile	Glu	Pro	Gln	Ser	Asn	Tyr	Ile	Pro	Glu	Thr	Pro	Pro	Pro	Gly	
	210						215					220					
10	TAT	ATC	AGT	GAA	GAT	GGA	GAA	ACA	AGT	GAC	CAA	CAG	TTG	AAT	CAA	AGT	720
	Tyr	Ile	Ser	Glu	Asp	Gly	Glu	Thr	Ser	Asp	Gln	Gln	Leu	Asn	Gln	Ser	
	225				230						235					240	
15	ATG	GAC	ACA	GGC	TCT	CCA	GCA	GAA	CTA	TCT	CCT	ACT	ACT	CTT	TCC	CCT	768
	Met	Asp	Thr	Gly	Ser	Pro	Ala	Glu	Leu	Ser	Pro	Thr	Thr	Leu	Ser	Pro	
					245						250					255	
20	GTT	AAT	CAT	AGC	TTG	GAT	TTA	CAG	CCA	GTT	ACT	TAC	TCA	GAA	CCT	GCA	816
	Val	Asn	His	Ser	Leu	Asp	Leu	Gln	Pro	Val	Thr	Tyr	Ser	Glu	Pro	Ala	
				260					265					270			
25	TTT	TGG	TGT	TCA	ATA	GCA	TAT	TAT	GAA	TTA	AAT	CAG	AGG	GTT	GGA	GAA	864
	Phe	Trp	Cys	Ser	Ile	Ala	Tyr	Tyr	Glu	Leu	Asn	Gln	Arg	Val	Gly	Glu	
			275					280					285				
30	ACC	TTC	CAT	GCA	TCA	CAG	CCC	TCA	CTC	ACT	GTA	GAT	GGC	TTT	ACA	GAC	912
	Thr	Phe	His	Ala	Ser	Gln	Pro	Ser	Leu	Thr	Val	Asp	Gly	Phe	Thr	Asp	
		290					295					300					
35	CCA	TCA	AAT	TCA	GAG	AGG	TTC	TGC	TTA	GGT	TTA	CTC	TCC	AAT	GTT	AAC	960
	Pro	Ser	Asn	Ser	Glu	Arg	Phe	Cys	Leu	Gly	Leu	Leu	Ser	Asn	Val	Asn	
	305					310					315					320	
40	CGA	AAT	GCC	ACG	GTA	GAA	ATG	ACA	AGA	AGG	CAT	ATA	GGA	AGA	GGA	GTG	1008
	Arg	Asn	Ala	Thr	Val	Glu	Met	Thr	Arg	Arg	His	Ile	Gly	Arg	Gly	Val	
					325					330					335		
45	CGC	TTA	TAC	TAC	ATA	GGT	GGG	GAA	GTT	TTT	GCT	GAG	TGC	CTA	AGT	GAT	1056
	Arg	Leu	Tyr	Tyr	Ile	Gly	Gly	Glu	Val	Phe	Ala	Glu	Cys	Leu	Ser	Asp	
				340					345					350			
50	AGT	GCA	ATC	TTT	GTG	CAG	AGC	CCC	AAT	TGT	AAT	CAG	AGA	TAT	GGC	TGG	1104
	Ser	Ala	Ile	Phe	Val	Gln	Ser	Pro	Asn	Cys	Asn	Gln	Arg	Tyr	Gly	Trp	
			355					360					365				
55	CAC	CCT	GCA	ACA	GTG	TGT	AAA	ATT	CCA	CCA	GGC	TGT	AAT	CTG	AAG	ATC	1152
	His	Pro	Ala	Thr	Val	Cys	Lys	Ile	Pro	Pro	Gly	Cys	Asn	Leu	Lys	Ile	
		370					375					380					
60	TTC	AAC	AAC	CAG	GAA	TTT	GCT	GCT	CTT	CTG	GCT	CAG	TCT	GTT	AAT	CAG	1200
	Phe	Asn	Asn	Gln	Glu	Phe	Ala	Ala	Leu	Leu	Ala	Gln	Ser	Val	Asn	Gln	
	385					390					395						
65	AGT	TTT	GTG	AAA	GGG	TGG	GGA	GCA	GAA	TAC	CGA	AGG	CAG	ACG	GTA	ACA	1296
	Ser	Phe	Val	Lys	Gly	Trp	Gly	Ala	Glu	Tyr	Arg	Arg	Gln	Thr	Val	Thr	
				420					425								

169

5	AGT ACT CCT TGC TGG ATT GAA CTT CAT CTG AAT GGA CCT CTA CAG TGG	1344
	Ser Thr Pro Cys Trp Ile Glu Leu His Leu Asn Gly Pro Leu Gln Trp	
	435 440 445	
10	TTG GAC AAA GTA TTA ACT CAG ATG GGA TCC CCT TCA GTG CGT TGC TCA	1392
	Leu Asp Lys Val Leu Thr Gln Met Gly Ser Pro Ser Val Arg Cys Ser	
	450 455 460	
15	AGC ATG TCA TGG GTA CCG CGG GCC CGG GAT CCA CCG GTC GCC ACC ATG	1440
	Ser Met Ser Trp Val Pro Arg Ala Arg Asp Pro Pro Val Ala Thr Met	
	465 470 475 480	
20	GTG AGC AAG CGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC	1488
	Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val	
	485 490 495	
25	GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG	1536
	Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu	
	500 505 510	
30	GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC	1584
	Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys	
	515 520 525	
35	ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG	1632
	Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu	
	530 535 540	
40	ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG	1680
	Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln	
	545 550 555 560	
45	CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC	1728
	His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg	
	565 570 575	
50	ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG	1776
	Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val	
	580 585 590	
55	AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC	1824
	Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile	
	595 600 605	
60	GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC	1872
	Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn	
	610 615 620	
65	ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG	1968
	Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val	
	645 650	

170

CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC 2016
 Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
 660 665 670
 5 GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC 2064
 Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
 675 680 685
 10 AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG 2112
 Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
 690 695 700
 15 ACC GCC CCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA 2157
 Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
 705 710 715

(2) INFORMATION FOR SEQ ID NO:75:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 718 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

25

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

Met Ser Ser Ile Leu Pro Phe Thr Pro Pro Val Val Lys Arg Leu Leu
 1 5 10 15
 Gly Trp Lys Lys Ser Ala Gly Gly Ser Gly Gly Ala Gly Gly Gly Glu
 20 25 30
 35 Gln Asn Gly Gln Glu Glu Lys Trp Cys Glu Lys Ala Val Lys Ser Leu
 35 40 45
 Val Lys Lys Leu Lys Lys Thr Gly Arg Leu Asp Glu Leu Glu Lys Ala
 50 55 60
 40 Ile Thr Thr Gln Asn Cys Asn Thr Lys Cys Val Thr Ile Pro Ser Thr
 65 70 75 80
 Cys Ser Glu Ile Trp Gly Leu Ser Thr Pro Asn Thr Ile Asp Gln Trp
 85 90 95
 Asp Thr Thr Gly Leu Tyr Ser Phe Ser Glu Gln Thr Arg Ser Leu Asp
 100 105 110
 45 Gly Arg Leu Gln Val Ser His Arg Lys Gly Leu Pro His Val Ile Tyr
 115 120 125
 Cys Arg Leu Trp Arg Trp Pro Asp Leu His Ser His His Glu Leu Lys
 130 135 140 145 150 155 160 165 170 175
 55 Pro Val Leu Val Pro Arg His Thr Glu Ile Leu Thr Glu Leu Pro Pro
 180 185 190
 Leu Asp Asp Tyr Thr His Ser Ile Pro Glu Asp Thr Asp Phe Ile Lys

			195					200					205				
	Gly	Ile	Glu	Pro	Gln	Ser	Asn	Tyr	Ile	Pro	Glu	Thr	Pro	Pro	Pro	Gly	
		210					215					220					
5	Tyr	Ile	Ser	Glu	Asp	Gly	Glu	Thr	Ser	Asp	Gln	Gln	Leu	Asn	Gln	Ser	
	225					230					235					240	
	Met	Asp	Thr	Gly	Ser	Pro	Ala	Glu	Leu	Ser	Pro	Thr	Thr	Leu	Ser	Pro	
					245					250					255		
	Val	Asn	His	Ser	Leu	Asp	Leu	Gln	Pro	Val	Thr	Tyr	Ser	Glu	Pro	Ala	
				260					265					270			
10	Phe	Trp	Cys	Ser	Ile	Ala	Tyr	Tyr	Glu	Leu	Asn	Gln	Arg	Val	Gly	Glu	
			275					280					285				
	Thr	Phe	His	Ala	Ser	Gln	Pro	Ser	Leu	Thr	Val	Asp	Gly	Phe	Thr	Asp	
		290				295						300					
15	Pro	Ser	Asn	Ser	Glu	Arg	Phe	Cys	Leu	Gly	Leu	Leu	Ser	Asn	Val	Asn	
	305					310					315					320	
	Arg	Asn	Ala	Thr	Val	Glu	Met	Thr	Arg	Arg	His	Ile	Gly	Arg	Gly	Val	
					325					330					335		
	Arg	Leu	Tyr	Tyr	Ile	Gly	Gly	Glu	Val	Phe	Ala	Glu	Cys	Leu	Ser	Asp	
				340					345					350			
20	Ser	Ala	Ile	Phe	Val	Gln	Ser	Pro	Asn	Cys	Asn	Gln	Arg	Tyr	Gly	Trp	
			355					360					365				
	His	Pro	Ala	Thr	Val	Cys	Lys	Ile	Pro	Pro	Gly	Cys	Asn	Leu	Lys	Ile	
		370					375					380					
25	Phe	Asn	Asn	Gln	Glu	Phe	Ala	Ala	Leu	Leu	Ala	Gln	Ser	Val	Asn	Gln	
	385					390					395					400	
	Gly	Phe	Glu	Ala	Val	Tyr	Gln	Leu	Thr	Arg	Met	Cys	Thr	Ile	Arg	Met	
					405					410					415		
	Ser	Phe	Val	Lys	Gly	Trp	Gly	Ala	Glu	Tyr	Arg	Arg	Gln	Thr	Val	Thr	
				420					425					430			
30	Ser	Thr	Pro	Cys	Trp	Ile	Glu	Leu	His	Leu	Asn	Gly	Pro	Leu	Gln	Trp	
			435					440					445				
	Leu	Asp	Lys	Val	Leu	Thr	Gln	Met	Gly	Ser	Pro	Ser	Val	Arg	Cys	Ser	
		450					455					460					
35	Ser	Met	Ser	Trp	Val	Pro	Arg	Ala	Arg	Asp	Pro	Pro	Val	Ala	Thr	Met	
	465					470					475					480	
	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	Val	
					485					490					495		
	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	Glu	
				500					505					510			
40	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Le					

SUBSTITUTE SHEET (RULE 26)

173

	Lys Tyr Cys Gln Tyr Ala Phe Asp Leu Lys Cys Asp Ser Val Cys Val	
	115 120 125	
5	AAT CCA TAT CAC TAC GAA CGA GTT GTA TCA CCT GGA ATT GAT CTC TCA Asn Pro Tyr His Tyr Glu Arg Val Ser Pro Gly Ile Asp Leu Ser	432
	130 135 140	
10	GGA TTA ACA CTG CAG AGT AAT GCT CCA TCA AGT ATG ATG GTG AAG GAT Gly Leu Thr Leu Gln Ser Asn Ala Pro Ser Ser Met Met Val Lys Asp	480
	145 150 155 160	
15	GAA TAT GTG CAT GAC TTT GAG GGA CAG CCA TCG TTG TCC ACT GAA GGA Glu Tyr Val His Asp Phe Glu Gly Gln Pro Ser Leu Ser Thr Glu Gly	528
	165 170 175	
	CAT TCA ATT CAA ACC ATC CAG CAT CCA CCA AGT AAT CGT GCA TCG ACA His Ser Ile Gln Thr Ile Gln His Pro Pro Ser Asn Arg Ala Ser Thr	576
	180 185 190	
20	GAG ACA TAC AGC ACC CCA GCT CTG TTA GCC CCA TCT GAG TCT AAT GCT Glu Thr Tyr Ser Thr Pro Ala Leu Leu Ala Pro Ser Glu Ser Asn Ala	624
	195 200 205	
25	ACC AGC ACT GCC AAC TTT CCC AAC ATT CCT GTG GCT TCC ACA AGT CAG Thr Ser Thr Ala Asn Phe Pro Asn Ile Pro Val Ala Ser Thr Ser Gln	672
	210 215 220	
30	CCT GCC AGT ATA CTG GGG GGC AGC CAT AGT GAA GGA CTG TTG CAG ATA Pro Ala Ser Ile Leu Gly Gly Ser His Ser Glu Gly Leu Leu Gln Ile	720
	225 230 235 240	
35	GCA TCA GGG CCT CAG CCA GGA CAG CAG CAG AAT GGA TTT ACT GGT CAG Ala Ser Gly Pro Gln Pro Gly Gln Gln Gln Asn Gly Phe Thr Gly Gln	768
	245 250 255	
	CCA GCT ACT TAC CAT CAT AAC AGC ACT ACC ACC TGG ACT GGA AGT AGG Pro Ala Thr Tyr His His Asn Ser Thr Thr Thr Trp Thr Gly Ser Arg	816
	260 265 270	
40	ACT GCA CCA TAC ACA CCT AAT TTG CCT CAC CAC CAA AAC GGC CAT CTT Thr Ala Pro Tyr Thr Pro Asn Leu Pro His His Gln Asn Gly His Leu	864
	275 280 285	
45	CAG CAC CAC CCG CCT ATG CCG CCC CAT CCC GGA CAT TAC TGG CCT GTT Gln His His Pro Pro Met Pro Pro His Pro Gly His Tyr Trp Pro Val	912
	290 295 300	
	CAC AAT GAG CTT GCA TTC CAG CCT CCC ATT TCC AAT CAT CCT GGT GGT His Asn Gln Tyr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr	
	305 310 315 320 325 330 335	
55	GAG ACA TTT AAG GTT CCT TCA AGC TCG CCT ATG GGT AAT GGT AAT GGT Glu Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr	
	325 330 335	

174

	Glu Thr Phe Lys Val Pro Ser Ser Cys Pro Ile Val Thr Val Asp Gly	
	340 345 350	
5	TAC GTG GAC CCT TCT GGA GGA GAT CGC TTT TGT TTG GGT CAA CTC TCC Tyr Val Asp Pro Ser Gly Gly Asp Arg Phe Cys Leu Gly Gln Leu Ser	1104
	355 360 365	
10	AAT GTC CAC AGG ACA GAA GCC ATT GAG AGA GCA AGG TTG CAC ATA GGC Asn Val His Arg Thr Glu Ala Ile Glu Arg Ala Arg Leu His Ile Gly	1152
	370 375 380	
15	AAA GGT GTG CAG TTG GAA TGT AAA GGT GAA GGT GAT GTT TGG GTC AGG Lys Gly Val Gln Leu Glu Cys Lys Gly Glu Gly Asp Val Trp Val Arg	1200
	385 390 395 400	
	TGC CTT AGT GAC CAC GCG GTC TTT GTA CAG AGT TAC TAC TTA GAC AGA Cys Leu Ser Asp His Ala Val Phe Val Gln Ser Tyr Tyr Leu Asp Arg	1248
	405 410 415	
20	GAA GCT GGG CGT GCA CCT GGA GAT GCT GTT CAT AAG ATC TAC CCA AGT Glu Ala Gly Arg Ala Pro Gly Asp Ala Val His Lys Ile Tyr Pro Ser	1296
	420 425 430	
25	GCA TAT ATA AAG GTC TTT GAT TTG CGT CAG TGT CAT CGA CAG ATG CAG Ala Tyr Ile Lys Val Phe Asp Leu Arg Gln Cys His Arg Gln Met Gln	1344
	435 440 445	
30	CAG CAG GCG GCT ACT GCA CAA GCT GCA GCA GCT GCC CAG GCA GCA GCC Gln Gln Ala Ala Thr Ala Gln Ala Ala Ala Ala Ala Gln Ala Ala Ala	1392
	450 455 460	
35	GTG GCA GGA AAC ATC CCT GGC CCA GGA TCA GTA GGT GGA ATA GCT CCA Val Ala Gly Asn Ile Pro Gly Pro Gly Ser Val Gly Gly Ile Ala Pro	1440
	465 470 475 480	
	GCT ATC AGT CTG TCA GCT GCT GCT GGA ATT GGT GTT GAT GAC CTT CGT Ala Ile Ser Leu Ser Ala Ala Ala Gly Ile Gly Val Asp Asp Leu Arg	1488
	485 490 495	
40	CGC TTA TGC ATA CTC AGG ATG AGT TTT GTG AAA GGC TGG GGA CCG GAT Arg Leu Cys Ile Leu Arg Met Ser Phe Val Lys Gly Trp Gly Pro Asp	1536
	500 505 510	
45	TAC CCA AGA CAG AGC ATC AAA GAA ACA CCT TGC TGG ATT GAA ATT CAC Tyr Pro Arg Gln Ser Ile Lys Glu Thr Pro Cys Trp Ile Glu Ile His	1584
	515 520 525	
	TTA CAC CGG GCC CTC CAG CTC CTA GAC GAA GAT GTT GAA GAA GAA	
	530 535 540 545 550 555 560	
55	TTA CAC CGG GCC CTC CAG CTC CTA GAC GAA GAT GTT GAA GAA GAA Tyr Pro Arg Gln Ser Ile Lys Glu Thr Pro Cys Trp Ile Glu Ile His	1632
	545 550 555 560	
	GTG AGC AAG GGC GAG GAG CTC TTT TTT TTT TTT TTT TTT TTT TTT	

175

	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	Val	
					565					570					575		
5	GAG	CTG	GAC	GGC	GAC	GTA	AAC	GGC	CAC	AAG	TTC	AGC	GTG	TCC	GGC	GAG	1776
	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	Glu	
				580					585					590			
10	GGC	GAG	GGC	GAT	GCC	ACC	TAC	GGC	AAG	CTG	ACC	CTG	AAG	TTC	ATC	TGC	1824
	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	Cys	
			595					600					605				
15	ACC	ACC	GGC	AAG	CTG	CCC	GTG	CCC	TGG	CCC	ACC	CTC	GTG	ACC	ACC	CTG	1872
	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	Leu	
			610				615					620					
	ACC	TAC	GGC	GTG	CAG	TGC	TTC	AGC	CGC	TAC	CCC	GAC	CAC	ATG	AAG	CAG	1920
	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	Gln	
	625				630					635						640	
20	CAC	GAC	TTC	TTC	AAG	TCC	GCC	ATG	CCC	GAA	GGC	TAC	GTC	CAG	GAG	CGC	1968
	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	Arg	
					645				650					655			
25	ACC	ATC	TTC	TTC	AAG	GAC	GAC	GGC	AAC	TAC	AAG	ACC	CGC	GCC	GAG	GTG	2016
	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	Val	
				660				665					670				
30	AAG	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	CGC	ATC	GAG	CTG	AAG	GGC	ATC	2064
	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	Ile	
			675				680					685					
35	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	CAC	AAG	CTG	GAG	TAC	AAC	2112
	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	Asn	
			690			695						700					
	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	GAC	AAG	CAG	AAG	AAC	GGC	2160
	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	Gly	
	705				710					715						720	
40	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	ATC	GAG	GAC	GGC	AGC	GTG	2208
	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	Val	
				725				730						735			
45	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	CCC	ATC	GGC	GAC	GGC	CCC	2256
	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	Pro	
			740					745					750				
	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	ACC	CAG	TCC	GGC	CTG		
	Val	Leu	Leu	Phe	Asp	Thr	Leu	Val	Asn	Gly	Val	Leu	Val	Leu	Glu	Phe	Val
55	ACC	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	CAG	CTG	TTC	GGC	CTG		

176

Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
 785 790 795

5 (2) INFORMATION FOR SEQ ID NO:77:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 798 amino acids

(B) TYPE: amino acid

10 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

Met Asp Asn Met Ser Ile Thr Asn Thr Pro Thr Ser Asn Asp Ala Cys
 1 5 10 15
 20 Leu Ser Ile Val His Ser Leu Met Cys His Arg Gln Gly Gly Glu Ser
 20 25 30
 Glu Thr Phe Ala Lys Arg Ala Ile Glu Ser Leu Val Lys Lys Leu Lys
 35 40 45
 25 Glu Lys Lys Asp Glu Leu Asp Ser Leu Ile Thr Ala Ile Thr Thr Asn
 50 55 60
 Gly Ala His Pro Ser Lys Cys Val Thr Ile Gln Arg Thr Leu Asp Gly
 65 70 75 80
 Arg Leu Gln Val Ala Gly Arg Lys Gly Phe Pro His Val Ile Tyr Ala
 85 90 95
 30 Arg Leu Trp Arg Trp Pro Asp Leu His Lys Asn Glu Leu Lys His Val
 100 105 110
 Lys Tyr Cys Gln Tyr Ala Phe Asp Leu Lys Cys Asp Ser Val Cys Val
 115 120 125
 35 Asn Pro Tyr His Tyr Glu Arg Val Val Ser Pro Gly Ile Asp Leu Ser
 130 135 140
 Gly Leu Thr Leu Gln Ser Asn Ala Pro Ser Ser Met Met Val Lys Asp
 145 150 155 160
 Glu Tyr Val His Asp Phe Glu Gly Gln Pro Ser Leu Ser Thr Glu Gly
 165 170 175
 40 His Ser Ile Gln Thr Ile Gln His Pro Pro Ser Asn Arg Ala Ser Thr
 180 185 190
 Glu Thr Tyr Ser Thr Pro Ala Leu Leu Ala Pro Ser Glu Ser Asn Ala
 195 200 205
 45 Thr Ser Thr Ala Asn Phe Pro Asn Ile Pro Val Ala Ser Thr Ser Gln
 210 215 220
 Pro Ala Ser Ile Leu Gly Gly Ser His Ser Glu Gly Leu Leu Gln Ile
 225 230 235 240
 Ala Ser Gly Pro Gln Pro Gly Gln Gln Gln Asn Gly Phe Thr Glu
 245 250 255 260 265 270 275 280 285
 55 Gln His His Pro Pro Met Pro Pro His Pro Gly His Tyr Trp Pro Val
 290 295 300
 His Asn Glu Leu Ala Phe Gln Pro Pro Ile Ser Asn His Thr Thr Thr

177

[illegible]

178

				755				760					765				
	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	Val	
		770					775					780					
	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys			
5		785				790						795					

(2) INFORMATION FOR SEQ ID NO:78:

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 3138 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

20 (A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...3135
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

ATG GCG GGC TGG ATC CAG GCC CAG CAG CTG CAG GGA GAC GCG CTG CGC
Met Ala Gly Trp Ile Gln Ala Gln Gln Leu Gln Gly Asp Ala Leu Arg

1 5 10 15

30 CAC ATG CAG GTG CTG TAC GGC CAG CAC TTC CCC ATC GAG GTC CGG CAC 96
Gln Met Gln Val Leu Tyr Gly Gln His Phe Pro Ile Glu Val Arg His
20 25 30

TAC TTG GCC CAG TGG ATT GAG AGC CAG CCA TGG GAT GCC ATT GAC TTG 144
Tyr Leu Ala Gln Trp Ile Glu Ser Gln Pro Trp Asp Ala Ile Asp Leu
35 40 45

GAC AAT CCC CAG GAC AGA GCC CAA GCC ACC CAG CTC CTG GAG GGC CTG 192
Asp Asn Pro Gln Asp Arg Ala Gln Ala Thr Gln Leu Leu Glu Gly Leu
50 55 60

40 GTG CAG GAG CTG CAG AAG AAG GCG GAG CAC CAG GTG GGG GAA GAT GGG 240
Val Gln Glu Leu Gln Lys Lys Ala Glu His Gln Val Gly Glu Asp Gly
65 70 75 80

45 TTT TTA CTG AAG ATC AAG CTG GGG CAC TAC GCC ACG CAG CTC CAG AAA 288
Phe Leu Leu Lys Ile Lys Leu Gly His Tyr Ala Thr Gln Leu Gln Lys
 85 90 95

ACA TAT GAC CGC TGC CCC CTG GAG CTG GTC CGC TGC ATC CCC GAG AATC

115 120 125

55 CCG GCT GGG ATC CTG GTT GAC GCC ATG TGG GAG AAC GAG GGT TTT AT

179

	Pro	Ala	Gly	Ile	Leu	Val	Asp	Ala	Met	Ser	Gln	Lys	His	Leu	Gln	Ile	
	130						135					140					
5	AAC	CAG	ACA	TTT	GAG	GAG	CTG	CGA	CTG	GTC	ACG	CAG	GAC	ACA	GAG	AAT	480
	Asn	Gln	Thr	Phe	Glu	Glu	Leu	Arg	Leu	Val	Thr	Gln	Asp	Thr	Glu	Asn	
	145				150					155					160		
10	GAG	CTG	AAG	AAA	CTG	CAG	CAG	ACT	CAG	GAG	TAC	TTC	ATC	ATC	CAG	TAC	528
	Glu	Leu	Lys	Lys	Leu	Gln	Gln	Thr	Gln	Glu	Tyr	Phe	Ile	Ile	Gln	Tyr	
					165					170					175		
15	CAG	GAG	AGC	CTG	AGG	ATC	CAA	GCT	CAG	TTT	GCC	CAG	CTG	GCC	CAG	CTG	576
	Gln	Glu	Ser	Leu	Arg	Ile	Gln	Ala	Gln	Phe	Ala	Gln	Leu	Ala	Gln	Leu	
				180					185					190			
20	AGC	CCC	CAG	GAG	CGT	CTG	AGC	CGG	GAG	ACG	GCC	CTC	CAG	CAG	AAG	CAG	624
	Ser	Pro	Gln	Glu	Arg	Leu	Ser	Arg	Glu	Thr	Ala	Leu	Gln	Gln	Lys	Gln	
			195					200					205				
25	GTG	TCT	CTG	GAG	GCC	TGG	TTG	CAG	CGT	GAG	GCA	CAG	ACA	CTG	CAG	CAG	672
	Val	Ser	Leu	Glu	Ala	Trp	Leu	Gln	Arg	Glu	Ala	Gln	Thr	Leu	Gln	Gln	
		210					215					220					
30	TAC	CGC	GTG	GAG	CTG	GCC	GAG	AAG	CAC	CAG	AAG	ACC	CTG	CAG	CTG	CTG	720
	Tyr	Arg	Val	Glu	Leu	Ala	Glu	Lys	His	Gln	Lys	Thr	Leu	Gln	Leu	Leu	
	225					230					235				240		
35	CGG	AAG	CAG	CAG	ACC	ATC	ATC	CTG	GAT	GAC	GAG	CTG	ATC	CAG	TGG	AAG	768
	Arg	Lys	Gln	Gln	Thr	Ile	Ile	Leu	Asp	Asp	Glu	Leu	Ile	Gln	Trp	Lys	
					245					250					255		
40	CGG	CGG	CAG	CAG	CTG	GCC	GGG	AAC	GGC	GGG	CCC	CCC	GAG	GGC	AGC	CTG	816
	Arg	Arg	Gln	Gln	Leu	Ala	Gly	Asn	Gly	Gly	Pro	Pro	Glu	Gly	Ser	Leu	
					260				265					270			
45	GAC	GTG	CTA	CAG	TCC	TGG	TGT	GAG	AAG	TTG	GCC	GAG	ATC	ATC	TGG	CAG	864
	Asp	Val	Leu	Gln	Ser	Trp	Cys	Glu	Lys	Leu	Ala	Glu	Ile	Ile	Trp	Gln	
		275						280					285				
50	AAC	CGG	CAG	CAG	ATC	CGC	AGG	GCT	GAG	CAC	CTC	TGC	CAG	CAG	CTG	CCC	912
	Asn	Arg	Gln	Gln	Ile	Arg	Arg	Ala	Glu	His	Leu	Cys	Gln	Gln	Leu	Pro	
		290					295					300					
55	ATC	CCC	GGC	CCA	GTG	GAG	GAG	ATG	CTG	GCC	GAG	GTC	AAC	GCC	ACC	ATC	960
	Ile	Pro	Gly	Pro	Val	Glu	Glu	Met	Leu	Ala	Glu	Val	Asn	Ala	Thr	Ile	
	305					310					315				320		
60	ACG	GAC	ATT	ATC	TCA	GCC	CTG	GTG	ACC	ACC	ACC	TTT	ATT	ATT	ATT	ATT	1008
65	AAA	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	1056
	Ala	Pro	Pro	Gln	Val	Leu	Lys	Thr	Gln	Thr	Lys	Phe	Ala	Ala	Thr	Val	
					340				345					350			
70	CGC	CTG	CTG	CTG	GCC	GCC	AGC	CTG	AAA	AAA	AAA	AAA	AAA	AAA	AAA	AAA	1104

	Arg	Leu	Leu	Val	Gly	Gly	Lys	Leu	Asn	Val	His	Met	Asn	Pro	Pro	Gln	
	355							360					365				
5	GTG	AAG	GCC	ACC	ATC	ATC	AGT	GAG	CAG	CAG	GCC	AAG	TCT	CTG	CTT	AAA	1152
	Val	Lys	Ala	Thr	Ile	Ile	Ser	Glu	Gln	Gln	Ala	Lys	Ser	Leu	Leu	Lys	
	370						375					380					
10	AAT	GAG	AAC	ACC	CGC	AAC	GAG	TGC	AGT	GGT	GAG	ATC	CTG	AAC	AAC	TGC	1200
	Asn	Glu	Asn	Thr	Arg	Asn	Glu	Cys	Ser	Gly	Glu	Ile	Leu	Asn	Asn	Cys	
	385					390					395					400	
15	TGC	GTG	ATG	GAG	TAC	CAC	CAA	GCC	ACG	GGC	ACC	CTC	AGT	GCC	CAC	TTC	1248
	Cys	Val	Met	Glu	Tyr	His	Gln	Ala	Thr	Gly	Thr	Leu	Ser	Ala	His	Phe	
					405					410					415		
20	AGG	AAC	ATG	TCA	CTG	AAG	AGG	ATC	AAG	CGT	GCT	GAC	CGG	CGG	GGT	GCA	1296
	Arg	Asn	Met	Ser	Leu	Lys	Arg	Ile	Lys	Arg	Ala	Asp	Arg	Arg	Gly	Ala	
				420					425					430			
25	GAG	TCC	GTG	ACA	GAG	GAG	AAG	TTC	ACA	GTC	CTG	TTT	GAG	TCT	CAG	TTC	1344
	Glu	Ser	Val	Thr	Glu	Glu	Lys	Phe	Thr	Val	Leu	Phe	Glu	Ser	Gln	Phe	
			435					440					445				
30	AGT	GTT	GGC	AGC	AAT	GAG	CTT	GTG	TTC	CAG	GTG	AAG	ACT	CTG	TCC	CTA	1392
	Ser	Val	Gly	Ser	Asn	Glu	Leu	Val	Phe	Gln	Val	Lys	Thr	Leu	Ser	Leu	
		450					455					460					
35	CCT	GTG	GTT	GTC	ATC	GTC	CAC	GGC	AGC	CAG	GAC	CAC	AAT	GCC	ACG	GCT	1440
	Pro	Val	Val	Val	Ile	Val	His	Gly	Ser	Gln	Asp	His	Asn	Ala	Thr	Ala	
	465					470					475					480	
40	ACT	GTG	CTG	TGG	GAC	AAT	GCC	TTT	GCT	GAG	CCG	GGC	AGG	GTG	CCA	TTT	1488
	Thr	Val	Leu	Trp	Asp	Asn	Ala	Phe	Ala	Glu	Pro	Gly	Arg	Val	Pro	Phe	
					485				490						495		
45	GCC	GTG	CCT	GAC	AAA	GTG	CTG	TGG	CCG	CAG	CTG	TGT	GAG	GCG	CTC	AAC	1536
	Ala	Val	Pro	Asp	Lys	Val	Leu	Trp	Pro	Gln	Leu	Cys	Glu	Ala	Leu	Asn	
				500					505					510			
50	ATG	AAA	TTC	AAG	GCC	GAA	GTG	CAG	AGC	AAC	CGG	GGC	CTG	ACC	AAG	GAG	1584
	Met	Lys	Phe	Lys	Ala	Glu	Val	Gln	Ser	Asn	Arg	Gly	Leu	Thr	Lys	Glu	
			515					520					525				
55	AAC	CTC	GTG	TTC	CTG	GCG	CAG	AAA	CTG	TTC	AAC	AAC	AGC	AGC	AGC	CAC	1632
	Asn	Leu	Val	Phe	Leu	Ala	Gln	Lys	Leu	Phe	Asn	Asn	Ser	Ser	Ser	His	
			530				535					540					
60	CTG	GAG	GAC	TAC	AGT	GGC	CTG	TCC	GTG	TCC	TCC	TCC	GAC	TTC	AAA	1680	
	Leu	Gln	Leu	Val	Arg	Gly	Trp	Asn	Tyr	Thr	Phe	Trp	Gln	Trp	Phe	Asp	

181

	Val	Met	Glu	Val	Leu	Lys	Lys	His	His	Lys	Pro	His	Trp	Asn	Asp	Gly	
				580						585						590	
5	GCC	ATC	CTA	GGT	TTT	GTG	AAT	AAG	CAA	CAG	GCC	CAC	GAC	CTG	CTC	ATC	1824
	Ala	Ile	Leu	Gly	Phe	Val	Asn	Lys	Gln	Gln	Ala	His	Asp	Leu	Leu	Ile	
			595					600					605				
10	AAC	AAG	CCC	GAC	GGG	ACC	TTC	TTG	TTG	CGC	TTT	AGT	GAC	TCA	GAA	ATC	1872
	Asn	Lys	Pro	Asp	Gly	Thr	Phe	Leu	Leu	Arg	Phe	Ser	Asp	Ser	Glu	Ile	
		610					615					620					
15	GGG	GGC	ATC	ACC	ATC	GCC	TGG	AAG	TTT	GAC	TCC	CCG	GAA	CGC	AAC	CTG	1920
	Gly	Gly	Ile	Thr	Ile	Ala	Trp	Lys	Phe	Asp	Ser	Pro	Glu	Arg	Asn	Leu	
	625					630					635					640	
	TGG	AAC	CTG	AAA	CCA	TTC	ACC	ACG	CGG	GAT	TTC	TCC	ATC	AGG	TCC	CTG	1968
	Trp	Asn	Leu	Lys	Pro	Phe	Thr	Thr	Arg	Asp	Phe	Ser	Ile	Arg	Ser	Leu	
					645					650					655		
20	GCT	GAC	CGG	CTG	GGG	GAC	CTG	AGC	TAT	CTC	ATC	TAT	GTG	TTT	CCT	GAC	2016
	Ala	Asp	Arg	Leu	Gly	Asp	Leu	Ser	Tyr	Leu	Ile	Tyr	Val	Phe	Pro	Asp	
				660					665					670			
25	CGC	CCC	AAG	GAT	GAG	GTC	TTC	TCC	AAG	TAC	TAC	ACT	CCT	GTG	CTG	GCT	2064
	Arg	Pro	Lys	Asp	Glu	Val	Phe	Ser	Lys	Tyr	Tyr	Thr	Pro	Val	Leu	Ala	
			675					680					685				
30	AAA	GCT	GTT	GAT	GGA	TAT	GTG	AAA	CCA	CAG	ATC	AAG	CAA	GTG	GTC	CCT	2112
	Lys	Ala	Val	Asp	Gly	Tyr	Val	Lys	Pro	Gln	Ile	Lys	Gln	Val	Val	Pro	
		690					695					700					
35	GAG	TTT	GTG	AAT	GCA	TCT	GCA	GAT	GCT	GGG	GGC	AGC	AGC	GCC	ACG	TAC	2160
	Glu	Phe	Val	Asn	Ala	Ser	Ala	Asp	Ala	Gly	Gly	Ser	Ser	Ala	Thr	Tyr	
	705					710				715					720		
	ATG	GAC	CAG	GCC	CCC	TCC	CCA	GCT	GTG	TGC	CCC	CAG	GCT	CCC	TAT	AAC	2208
	Met	Asp	Gln	Ala	Pro	Ser	Pro	Ala	Val	Cys	Pro	Gln	Ala	Pro	Tyr	Asn	
					725					730					735		
40	ATG	TAC	CCA	CAG	AAC	CCT	GAC	CAT	GTA	CTC	GAT	CAG	GAT	GGA	GAA	TTC	2256
	Met	Tyr	Pro	Gln	Asn	Pro	Asp	His	Val	Leu	Asp	Gln	Asp	Gly	Glu	Phe	
				740					745					750			
45	GAC	CTG	GAT	GAG	ACC	ATG	GAT	GTG	GCC	AGG	CAC	GTG	GAG	GAA	CTC	TTA	2304
	Asp	Leu	Asp	Glu	Thr	Met	Asp	Val	Ala	Arg	His	Val	Glu	Glu	Leu	Leu	
			755					760					765				
	CGC	CGA	CCA	ATG	GAC	AGT	CTT	GAC	TCC	CGC	CTC	TCC	CGC	GCT	CGC	CGC	
	Arg	Arg	Pro	Met	Ala												
55	GAT	CCA	CCG	GTC	GCC	ACC	ATG	GTG	AGC	AAG	CCC	GAC	GAT	GAA	CTC	TTA	

[illegible]

183

Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met
 1025 1030 1035 1040

5 GAC GAG CTG TAC AAG TAA
 Asp Glu Leu Tyr Lys
 1045

3138

(2) INFORMATION FOR SEQ ID NO:79:

10

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1045 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

15

- (ii) MOLECULE TYPE: protein
 (v) FRAGMENT TYPE: internal

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:

Met Ala Gly Trp Ile Gln Ala Gln Gln Leu Gln Gly Asp Ala Leu Arg
 1 5 10 15
 25 Gln Met Gln Val Leu Tyr Gly Gln His Phe Pro Ile Glu Val Arg His
 20 25 30
 Tyr Leu Ala Gln Trp Ile Glu Ser Gln Pro Trp Asp Ala Ile Asp Leu
 35 40 45
 Asp Asn Pro Gln Asp Arg Ala Gln Ala Thr Gln Leu Leu Glu Gly Leu
 50 55 60
 30 Val Gln Glu Leu Gln Lys Lys Ala Glu His Gln Val Gly Glu Asp Gly
 65 70 75 80
 Phe Leu Leu Lys Ile Lys Leu Gly His Tyr Ala Thr Gln Leu Gln Lys
 85 90 95
 35 Thr Tyr Asp Arg Cys Pro Leu Glu Leu Val Arg Cys Ile Arg His Ile
 100 105 110
 Leu Tyr Asn Glu Gln Arg Leu Val Arg Glu Ala Asn Asn Cys Ser Ser
 115 120 125
 Pro Ala Gly Ile Leu Val Asp Ala Met Ser Gln Lys His Leu Gln Ile
 130 135 140
 40 Asn Gln Thr Phe Glu Glu Leu Arg Leu Val Thr Gln Asp Thr Glu Asn
 145 150 155 160
 Glu Leu Lys Lys Leu Gln Gln Thr Gln Glu Tyr Phe Ile Ile Gln Tyr
 165 170 175
 45 Gln Glu Ser Leu Arg Ile Gln Ala Gln Phe Ala Gln Leu Ala Gln Leu
 180 185 190
 Ser Pro Gln Glu Arg Leu Ser Arg Glu Thr Ala Leu Gln Gln Lys Gln
 195 200 205
 Val Ser Leu Glu Ala Trp Leu Gln Arg Gly Ala Gln Thr Leu Glu
 210 215 220 225 230 235 240 245
 55 Arg Arg Gln Gln Leu Ala Gly Asn Gly Gly Pro Pro Glu Gly Ser Leu
 260 265 270
 Asp Val Leu Gln Ser Trp Cys Gln Leu Leu Ala Thr Thr Thr Thr Thr

184

	275		280		285
	Asn Arg Gln Gln Ile Arg Arg Ala Glu His Leu Cys Gln Gln Leu Pro				
	290		295		300
5	Ile Pro Gly Pro Val Glu Glu Met Leu Ala Glu Val Asn Ala Thr Ile				
	305		310		315
	Thr Asp Ile Ile Ser Ala Leu Val Thr Ser Thr Phe Ile Ile Glu Lys				320
		325		330	
	Gln Pro Pro Gln Val Leu Lys Thr Gln Thr Lys Phe Ala Ala Thr Val				335
		340		345	
10	Arg Leu Leu Val Gly Gly Lys Leu Asn Val His Met Asn Pro Pro Gln				350
		355		360	
	Val Lys Ala Thr Ile Ile Ser Glu Gln Gln Ala Lys Ser Leu Leu Lys				365
		370		375	
	Asn Glu Asn Thr Arg Asn Glu Cys Ser Gly Glu Ile Leu Asn Asn Cys				380
15	385		390		395
	Cys Val Met Glu Tyr His Gln Ala Thr Gly Thr Leu Ser Ala His Phe				400
		405		410	
	Arg Asn Met Ser Leu Lys Arg Ile Lys Arg Ala Asp Arg Arg Gly Ala				415
		420		425	
20	Glu Ser Val Thr Glu Glu Lys Phe Thr Val Leu Phe Glu Ser Gln Phe				430
		435		440	
	Ser Val Gly Ser Asn Glu Leu Val Phe Gln Val Lys Thr Leu Ser Leu				445
		450		455	
	Pro Val Val Val Ile Val His Gly Ser Gln Asp His Asn Ala Thr Ala				460
25	465		470		475
	Thr Val Leu Trp Asp Asn Ala Phe Ala Glu Pro Gly Arg Val Pro Phe				480
		485		490	
	Ala Val Pro Asp Lys Val Leu Trp Pro Gln Leu Cys Glu Ala Leu Asn				495
		500		505	
30	Met Lys Phe Lys Ala Glu Val Gln Ser Asn Arg Gly Leu Thr Lys Glu				510
		515		520	
	Asn Leu Val Phe Leu Ala Gln Lys Leu Phe Asn Asn Ser Ser Ser His				525
		530		535	
	Leu Glu Asp Tyr Ser Gly Leu Ser Val Ser Trp Ser Gln Phe Asn Arg				540
35	545		550		555
	Glu Asn Leu Pro Gly Trp Asn Tyr Thr Phe Trp Gln Trp Phe Asp Gly				560
		565		570	
	Val Met Glu Val Leu Lys Lys His His Lys Pro His Trp Asn Asp Gly				575
		580		585	
40	Ala Ile Leu Gly Phe Val Asn Lys Gln Gln Ala His Asp Leu Leu Ile				590
		595		600	
	Asn Lys Pro Asp Gly Thr Phe Leu Leu Arg Phe Ser Asp Ser Glu Ile				605
		610		615	
	Gly Gly Ile Thr Ile Ala Trp Lys Phe Asp Ser Pro Glu Arg Asn Leu				620
45	625		630		635
	Trp Asn Leu Lys Pro Phe Thr Thr Arg Asp Phe Ser Ile Arg Ser Leu				640
		645		650	
	Ala Asp Arg Leu Gly Asp Leu Ser Tyr Leu Ile Thr Val Val Pro				655
		660		665	
		670		675	
		680		685	
		690		695	
		700		705	
55	Glu Phe Val Asn Ala Ser Ala Asp Ala Gly Gly Ser Ser Ala Thr Tyr				710
		715		720	
	Met Asp Gln Ala Pro Ser Pro Ala Val Ser Ser Thr Thr Thr Thr				725

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:
GTCTCGAGGG AGCATGGGCA CCTTGGC 27
- (2) INFORMATION FOR SEQ ID NO:82:
- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:
TGGGATCCGA GAAGTCTATA TCCCATC 27
- (2) INFORMATION FOR SEQ ID NO:83:
- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:
TGGGATCCTT AGAAGTCTAT ATCCCATC 28
- (2) INFORMATION FOR SEQ ID NO:84:
- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:
TGGGATCCTT AGAAGTCTAT ATCCCATC 28
- (2) INFORMATION FOR SEQ ID NO:85:
- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid

187

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:
GTGAATTCTC GTCTGATTTC TGGCAGGAGG 30
- (2) INFORMATION FOR SEQ ID NO:86:
- 10 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
15 (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:
20 GTGAATTCTT TACGTCTGAT TTCTGGCAGG 30
- (2) INFORMATION FOR SEQ ID NO:87:
- 25 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 34 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
- 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:
GTCTCGAGCC ATGGACGAAC TGTCCCCCT CATC 34
- 35 (2) INFORMATION FOR SEQ ID NO:88:
- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
40 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:
45 GTGGATCCAA GGAGCTGATC TGA CT CAGCA G 31
- (2) INFORMATION FOR SEQ ID NO:89:
- 55 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

188

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

GTGGATCCTT AGGAGCTGAT CTGACTCAGC AG

32

5 (2) INFORMATION FOR SEQ ID NO:90:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 32 base pairs

(B) TYPE: nucleic acid

10 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

15

CCTCCTAAGC TTATCATGGA CCATTATGAT TC

32

(2) INFORMATION FOR SEQ ID NO:91:

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

25 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

30 CCTCCTGGAT CCCTGCGCAG GATGATGGTC CAG

33

(2) INFORMATION FOR SEQ ID NO:92:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 45 base pairs

35 (B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

GGATGGAAGC TTCAATGGCT GCCATCCGGA AGAAACTGGT GATTG

45

(2) INFORMATION FOR SEQ ID NO:93:

45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 45 base pairs

(B) TYPE: nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

55 GGATGGGGAT CCTCACAAGA CAAGGCAACC AGATTTTTC TTCCC

45

189

(2) INFORMATION FOR SEQ ID NO:94:

(i) SEQUENCE CHARACTERISTICS:

5

- (A) LENGTH: 29 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

GGGAAGCTTC CATGAGCGAG ACGGTCATC

29

15

(2) INFORMATION FOR SEQ ID NO:95:

(i) SEQUENCE CHARACTERISTICS:

20

- (A) LENGTH: 28 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

25

CCCGGATCCT CAGGGAGAAC CCCGCTTC

28

(2) INFORMATION FOR SEQ ID NO:96:

(i) SEQUENCE CHARACTERISTICS:

30

- (A) LENGTH: 30 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

GTGAATTCGA CCATGGAGCG GCCCCCGGGG

30

40

(2) INFORMATION FOR SEQ ID NO:97:

(i) SEQUENCE CHARACTERISTICS:

45

- (A) LENGTH: 27 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(2) INFORMATION FOR SEQ ID NO:98:

55

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 28 base pairs

190

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

GTGGTACCTC ATTCTGTAA CCAACTCC

28

10

(2) INFORMATION FOR SEQ ID NO:99:

(i) SEQUENCE CHARACTERISTICS:

15

- (A) LENGTH: 28 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

20

GTCTCGAGAG ATGCTGTCCC GTGGGTGG

28

(2) INFORMATION FOR SEQ ID NO:100:

25

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 27 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

GTGAATTCGC TTCCTCTTGA GGGAACC

35

27

(2) INFORMATION FOR SEQ ID NO:101:

(i) SEQUENCE CHARACTERISTICS:

40

- (A) LENGTH: 27 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

GTGAATTCAC TTCCTCTTGA GGGAACC

27

(2) INFORMATION FOR SEQ ID NO:102:

50

TYPE: nucleic acid

55

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:
- 5 GTCTCGAGCC ATGGAGAACT TCCAAAAGG 29
- (2) INFORMATION FOR SEQ ID NO:103:
- (i) SEQUENCE CHARACTERISTICS:
- 10 (A) LENGTH: 28 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:
- GTGGATCCCA GAGTCGAAGA TGGGGTAC 28
- (2) INFORMATION FOR SEQ ID NO:104:
- 20 (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 29 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- 25 (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:
- 30 GTGGATCCTC AGAGTCGAAG ATGGGGTAC 29
- (2) INFORMATION FOR SEQ ID NO:105:
- (i) SEQUENCE CHARACTERISTICS:
- 35 (A) LENGTH: 30 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:
- GTGAATTCGG CGATGCCAGA CCCCGCGGCG 30
- 45 (2) INFORMATION FOR SEQ ID NO:106:
- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 32 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- 55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:
- GTGGATCCCA GGCACAGGCA GCCTCAGCCT TC

193

	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	
				100					105					110			
5	GTG	AAG	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	CGC	ATC	GAG	CTG	AAG	GGC	384
	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	
			115					120					125				
10	ATC	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	CAC	AAG	CTG	GAG	TAC	432
	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	
			130				135					140					
15	AAC	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	GAC	AAG	CAG	AAG	AAC	480
	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	
						150					155					160	
20	GGC	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	ATC	GAG	GAC	GGC	AGC	528
	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	
					165				170						175		
25	GTG	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	CCC	ATC	GGC	GAC	GGC	576
	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	
				180				185						190			
30	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	ACC	CAG	TCC	GCC	CTG	624
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	
			195				200					205					
35	AGC	AAA	GAC	CCC	AAC	GAG	AAG	CGC	GAT	CAC	ATG	GTC	CTG	CTG	GAG	TTC	672
	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	
		210					215					220					
40	GTG	ACC	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	GAG	CTG	TAC	AAG	TCC	720
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser	
		225				230					235					240	
45	GGA	CTC	AGA	TCT	CGA	GCT	CAA	GCT	TCG	AAT	TCG	GCG	ATG	CCA	GAC	CCC	768
	Gly	Leu	Arg	Ser	Arg	Ala	Gln	Ala	Ser	Asn	Ser	Ala	Met	Pro	Asp	Pro	
					245				250						255		
50	GCG	GCG	CAC	CTG	CCC	TTC	TTC	TAC	GGC	AGC	ATC	TCG	CGT	GCC	GAG	GCC	816
	Ala	Ala	His	Leu	Pro	Phe	Phe	Tyr	Gly	Ser	Ile	Ser	Arg	Ala	Glu	Ala	
				260				265						270			
55	GAG	GAG	CAC	CTG	AAG	CTG	GCG	GGC	ATG	GCG	GAC	GGG	CTC	TTC	CTG	CTG	864
	Glu	Glu	His	Leu	Lys	Leu	Ala	Gly	Met	Ala	Asp	Gly	Leu	Phe	Leu	Leu	
			275				280					285					
60	CGC	CAG	TGC	CTG	CGC	TCG	CTG	GGC	GGC	TAT	GTG	CTG	TCG	CTC	CTC	CAC	912
	Arg	Gln	Cys	Leu	Arg	Ala	Ala	Ala	Ala	Ile	Glu	Arg	Gln	Leu	Asn	Gly	

	Tyr	Ala	Ile	Ala	Gly	Gly	Lys	Ala	His	Cys	Gly	Pro	Ala	Glu	Leu	Cys	
					325					330					335		
5	GAG	TTC	TAC	TCG	CGC	GAC	CCC	GAC	GGG	CTG	CCC	TGC	AAC	CTG	CGC	AAG	1056
	Glu	Phe	Tyr	Ser	Arg	Asp	Pro	Asp	Gly	Leu	Pro	Cys	Asn	Leu	Arg	Lys	
				340					345					350			
10	CCG	TGC	AAC	CGG	CCG	TCG	GGC	CTC	GAG	CCG	CAG	CCG	GGG	GTC	TTC	GAC	1104
	Pro	Cys	Asn	Arg	Pro	Ser	Gly	Leu	Glu	Pro	Gln	Pro	Gly	Val	Phe	Asp	
				355				360					365				
15	TGC	CTG	CGA	GAC	GCC	ATG	GTG	CGT	GAC	TAC	GTG	CGC	CAG	ACG	TGG	AAG	1152
	Cys	Leu	Arg	Asp	Ala	Met	Val	Arg	Asp	Tyr	Val	Arg	Gln	Thr	Trp	Lys	
				370			375					380					
20	CTG	GAG	GGC	GAG	GCC	CTG	GAG	CAG	GCC	ATC	ATC	AGC	CAG	GCC	CCG	CAG	1200
	Leu	Glu	Gly	Glu	Ala	Leu	Glu	Gln	Ala	Ile	Ile	Ser	Gln	Ala	Pro	Gln	
	385					390				395						400	
25	GTG	GAG	AAG	CTC	ATT	GCT	ACG	ACG	GCC	CAC	GAG	CGG	ATG	CCC	TGG	TAC	1248
	Val	Glu	Lys	Leu	Ile	Ala	Thr	Thr	Ala	His	Glu	Arg	Met	Pro	Trp	Tyr	
					405				410						415		
30	CAC	AGC	AGC	CTG	ACG	CGT	GAG	GAG	GCC	GAG	CGC	AAA	CTT	TAC	TCT	GGG	1296
	His	Ser	Ser	Leu	Thr	Arg	Glu	Glu	Ala	Glu	Arg	Lys	Leu	Tyr	Ser	Gly	
				420					425					430			
35	GCG	CAG	ACC	GAC	GGC	AAG	TTC	CTG	CTG	AGG	CCG	CGG	AAG	GAG	CAG	GGC	1344
	Ala	Gln	Thr	Asp	Gly	Lys	Phe	Leu	Leu	Arg	Pro	Arg	Lys	Glu	Gln	Gly	
				435				440					445				
40	ACA	TAC	GCC	CTG	TCC	CTC	ATC	TAT	GGG	AAG	ACG	GTG	TAC	CAC	TAC	CTC	1392
	Thr	Tyr	Ala	Leu	Ser	Leu	Ile	Tyr	Gly	Lys	Thr	Val	Tyr	His	Tyr	Leu	
				450			455					460					
45	ATC	AGC	CAA	GAC	AAG	GCG	GGC	AAG	TAC	TGC	ATT	CCC	GAG	GGC	ACC	AAG	1440
	Ile	Ser	Gln	Asp	Lys	Ala	Gly	Lys	Tyr	Cys	Ile	Pro	Glu	Gly	Thr	Lys	
	465					470				475						480	
50	TTT	GAC	ACG	CTC	TGG	CAG	CTG	GTG	GAG	TAT	CTG	AAG	CTG	AAG	GCG	GAC	1488
	Phe	Asp	Thr	Leu	Trp	Gln	Leu	Val	Glu	Tyr	Leu	Lys	Leu	Lys	Ala	Asp	
					485				490								

195

	Thr	Pro	Glu	Pro	Ala	Arg	Ile	Thr	Ser	Pro	Asp	Lys	Pro	Arg	Pro	Met	
	545					550					555					560	
5	CCC	ATG	GAC	ACG	AGC	GTG	TAT	GAG	AGC	CCC	TAC	AGC	GAC	CCA	GAG	GAG	1728
	Pro	Met	Asp	Thr	Ser	Val	Tyr	Glu	Ser	Pro	Tyr	Ser	Asp	Pro	Glu	Glu	
					565					570					575		
10	CTC	AAG	GAC	AAG	AAG	CTC	TTC	CTG	AAG	CGC	GAT	AAC	CTC	CTC	ATA	GCT	1776
	Leu	Lys	Asp	Lys	Lys	Leu	Phe	Leu	Lys	Arg	Asp	Asn	Leu	Leu	Ile	Ala	
				580					585					590			
15	GAC	ATT	GAA	CTT	GGC	TGC	GGC	AAC	TTT	GGC	TCA	GTG	CGC	CAG	GGC	GTG	1824
	Asp	Ile	Glu	Leu	Gly	Cys	Gly	Asn	Phe	Gly	Ser	Val	Arg	Gln	Gly	Val	
			595				600					605					
20	TAC	CGC	ATG	CGC	AAG	AAG	CAG	ATC	GAC	GTG	GCC	ATC	AAG	GTG	CTG	AAG	1872
	Tyr	Arg	Met	Arg	Lys	Lys	Gln	Ile	Asp	Val	Ala	Ile	Lys	Val	Leu	Lys	
	610						615					620					
25	CAG	GGC	ACG	GAG	AAG	GCA	GAC	ACG	GAA	GAG	ATG	ATG	CGC	GAG	GCG	CAG	1920
	Gln	Gly	Thr	Glu	Lys	Ala	Asp	Thr	Glu	Glu	Met	Met	Arg	Glu	Ala	Gln	
	625					630					635				640		
30	ATC	ATG	CAC	CAG	CTG	GAC	AAC	CCC	TAC	ATC	GTG	CGG	CTC	ATT	GGC	GTC	1968
	Ile	Met	His	Gln	Leu	Asp	Asn	Pro	Tyr	Ile	Val	Arg	Leu	Ile	Gly	Val	
					645					650					655		
35	TGC	CAG	GCC	GAG	GCC	CTC	ATG	CTG	GTC	ATG	GAG	ATG	GCT	GGG	GGC	GGG	2016
	Cys	Gln	Ala	Glu	Ala	Leu	Met	Leu	Val	Met	Glu	Met	Ala	Gly	Gly	Gly	
				660					665					670			
40	CCG	CTG	CAC	AAG	TTC	CTG	GTC	GGC	AAG	AGG	GAG	GAG	ATC	CCT	GTG	AGC	2064
	Pro	Leu	His	Lys	Phe	Leu	Val	Gly	Lys	Arg	Glu	Glu	Ile	Pro	Val	Ser	
			675					680					685				
45	AAT	GTG	GCC	GAG	CTG	CTG	CAC	CAG	GTG	TCC	ATG	GGG	ATG	AAG	TAC	CTG	2112
	Asn	Val	Ala	Glu	Leu	Leu	His	Gln	Val	Ser	Met	Gly	Met	Lys	Tyr	Leu	
	690					695					700						
50	GAG	GAG	AAG	AAC	TTT	GTG	CAC	CGT	GAC	CTG	GCG	GCC	CGC	AAC	GTC	CTG	2160
	Glu	Glu	Lys	Asn	Phe	Val	His	Arg	Asp	Leu	Ala	Ala	Arg	Asn	Val	Leu	
	705					710					715				720		
55	CTG	GTT	AAC	CGG	CAC	TAC	GCC	AAG	ATC	AGC	GAC	TTT	GGC	CTC	TCC	AAA	2208
	Leu	Val	Asn	Arg	His	Tyr	Ala	Lys	Ile	Ser	Asp	Phe	Gly	Leu	Ser	Lys	
					725					730					735		
60	TGG	CCG	CTC	AAG	TGG	TAC	GCA	CCC	GAA	TGC	ATC	AAC	TTC	CGC	AAG	TTC	2304
	Trp	Pro	Leu	Lys	Trp	Tyr	Ala	Pro	Glu	Cys	Ile	Asn	Phe	Arg	Lys	Phe	
				755				760					765				

55

195

196

[illegible]

(2) INFORMATION FOR SEQ ID NO:109:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 871 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

35

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

45 Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
1 5 10 15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
20 25 30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
35 40 45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr
50

[illegible]

198

565 570 575
 Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg Asp Asn Leu Leu Ile Ala
 580 585 590
 Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val Arg Gln Gly Val
 595 600 605
 Tyr Arg Met Arg Lys Lys Gln Ile Asp Val Ala Ile Lys Val Leu Lys
 610 615 620
 Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu Met Met Arg Glu Ala Gln
 625 630 635 640
 10 Ile Met His Gln Leu Asp Asn Pro Tyr Ile Val Arg Leu Ile Gly Val
 645 650 655
 Cys Gln Ala Glu Ala Leu Met Leu Val Met Glu Met Ala Gly Gly Gly
 660 665 670
 Pro Leu His Lys Phe Leu Val Gly Lys Arg Glu Glu Ile Pro Val Ser
 675 680 685
 15 Asn Val Ala Glu Leu Leu His Gln Val Ser Met Gly Met Lys Tyr Leu
 690 695 700
 Glu Glu Lys Asn Phe Val His Arg Asp Leu Ala Ala Arg Asn Val Leu
 705 710 715 720
 20 Leu Val Asn Arg His Tyr Ala Lys Ile Ser Asp Phe Gly Leu Ser Lys
 725 730 735
 Ala Leu Gly Ala Asp Asp Ser Tyr Tyr Thr Ala Arg Ser Ala Gly Lys
 740 745 750
 Trp Pro Leu Lys Trp Tyr Ala Pro Glu Cys Ile Asn Phe Arg Lys Phe
 755 760 765
 25 Ser Ser Arg Ser Asp Val Trp Ser Tyr Gly Val Thr Met Trp Glu Ala
 770 775 780
 Leu Ser Tyr Gly Gln Lys Pro Tyr Lys Lys Met Lys Gly Pro Glu Val
 785 790 795 800
 30 Met Ala Phe Ile Glu Gln Gly Lys Arg Met Glu Cys Pro Pro Glu Cys
 805 810 815
 Pro Pro Glu Leu Tyr Ala Leu Met Ser Asp Cys Trp Ile Tyr Lys Trp
 820 825 830
 Glu Asp Arg Pro Asp Phe Leu Thr Val Glu Gln Arg Met Arg Ala Cys
 835 840 845
 35 Tyr Tyr Ser Leu Ala Ser Lys Val Glu Gly Pro Pro Gly Ser Thr Gln
 850 855 860
 Lys Ala Glu Ala Ala Cys Ala
 865 870
 40

(2) INFORMATION FOR SEQ ID NO:110:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2598 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULAR WEIGHT:

Molecular Weight: 1712598

LOCUS: 1712598

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110

199

5	ATG CCA GAC CCC GCG GCG CAC CTG CCC TTC TTC TAC GGC AGC ATC TCG Met Pro Asp Pro Ala Ala His Leu Pro Phe Phe Tyr Gly Ser Ile Ser 1 5 10 15	48
10	CGT GCC GAG GCC GAG GAG CAC CTG AAG CTG GCG GGC ATG GCG GAC GGG Arg Ala Glu Ala Glu Glu His Leu Lys Leu Ala Gly Met Ala Asp Gly 20 25 30	96
15	CTC TTC CTG CTG CGC CAG TGC CTG CGC TCG CTG GGC GGC TAT GTG CTG Leu Phe Leu Leu Arg Gln Cys Leu Arg Ser Leu Gly Gly Tyr Val Leu 35 40 45	144
20	TCG CTC GTG CAC GAT GTG CGC TTC CAC CAC TTT CCC ATC GAG CGC CAG Ser Leu Val His Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln 50 55 60	192
25	CTC AAC GGC ACC TAC GCC ATT GCC GGC GGC AAA GCG CAC TGT GGA CCG Leu Asn Gly Thr Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro 65 70 75 80	240
30	GCA GAG CTC TGC GAG TTC TAC TCG CGC GAC CCC GAC GGG CTG CCC TGC Ala Glu Leu Cys Glu Phe Tyr Ser Arg Asp Pro Asp Gly Leu Pro Cys 85 90 95	288
35	AAC CTG CGC AAG CCG TGC AAC CGG CCG TCG GGC CTC GAG CCG CAG CCG Asn Leu Arg Lys Pro Cys Asn Arg Pro Ser Gly Leu Glu Pro Gln Pro 100 105 110	336
40	GGG GTC TTC GAC TGC CTG CGA GAC GCC ATG GTG CGT GAC TAC GTG CGC Gly Val Phe Asp Cys Leu Arg Asp Ala Met Val Arg Asp Tyr Val Arg 115 120 125	384
45	CAG ACG TGG AAG CTG GAG GGC GAG GCC CTG GAG CAG GCC ATC ATC AGC Gln Thr Trp Lys Leu Glu Gly Glu Ala Leu Glu Gln Ala Ile Ile Ser 130 135 140	432
50	CAG GCC CCG CAG GTG GAG AAG CTC ATT GCT ACG ACG GCC CAC GAG CCG Gln Ala Pro Gln Val Glu Lys Leu Ile Ala Thr Thr Ala His Glu Arg 145 150 155 160	480
55	ATG CCC TGG TAC CAC AGC AGC CTG ACG CGT GAG GAG GCC GAG CGC AAA Met Pro Trp Tyr His Ser Ser Leu Thr Arg Glu Glu Ala Glu Arg Lys 165 170 175	528
60	CTT TAC TCT GGG GCG CAG ACC GAC GGC AAG TTC CTG CTG AGG CCG CCG Leu Tyr Ser Gly Ala Gln Thr Asp Gly Lys Phe Leu Leu Arg Pro Arg 180 185 190	576
65	TAC CAC TAC CTC ATC AGC CAA GAC AAG GCG GGC AAG TAC TGC ATT CCC Tyr His Tyr Leu Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro 210 215 220	672

200

5	GAG GGC ACC AAG TTT GAC ACG CTC TGG CAG CTG GTG GAG TAT CTG AAG	720
	Glu Gly Thr Lys Phe Asp Thr Leu Trp Gln Leu Val Glu Tyr Leu Lys	
	225 230 235 240	
10	CTG AAG GCG GAC GGG CTC ATC TAC TGC CTG AAG GAG GCC TGC CCC AAC	768
	Leu Lys Ala Asp Gly Leu Ile Tyr Cys Leu Lys Glu Ala Cys Pro Asn	
	245 250 255	
15	AGC AGT GCC AGC AAC GCC TCA GGG GCT GCT GCT CCC ACA CTC CCA GCC	816
	Ser Ser Ala Ser Asn Ala Ser Gly Ala Ala Ala Pro Thr Leu Pro Ala	
	260 265 270	
20	CAC CCA TCC ACC TTC ACT CAT CCT CAG AGA CGA ATC GAC ACC CTC AAC	864
	His Pro Ser Thr Leu Thr His Pro Gln Arg Arg Ile Asp Thr Leu Asn	
	275 280 285	
25	TCA GAT GGA TAC ACC CCT GAG CCA GCA CGC ATA ACG TCC CCA GAC AAA	912
	Ser Asp Gly Tyr Thr Pro Glu Pro Ala Arg Ile Thr Ser Pro Asp Lys	
	290 295 300	
30	CCG CGG CCG ATG CCC ATG GAC ACG AGC GTG TAT GAG AGC CCC TAC AGC	960
	Pro Arg Pro Met Pro Met Asp Thr Ser Val Tyr Glu Ser Pro Tyr Ser	
	305 310 315 320	
35	GAC CCA GAG GAG CTC AAG GAC AAG AAG CTC TTC CTG AAG CGC GAT AAC	1008
	Asp Pro Glu Glu Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg Asp Asn	
	325 330 335	
40	CTC CTC ATA GCT GAC ATT GAA CTT GGC TGC GGC AAC TTT GGC TCA GTG	1056
	Leu Leu Ile Ala Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val	
	340 345 350	
45	CGC CAG GGC GTG TAC CGC ATG CGC AAG AAG CAG ATC GAC GTG GCC ATC	1104
	Arg Gln Gly Val Tyr Arg Met Arg Lys Lys Gln Ile Asp Val Ala Ile	
	355 360 365	
50	AAG GTG CTG AAG CAG GGC ACG GAG AAG GCA GAC ACG GAA GAG ATG ATG	1152
	Lys Val Leu Lys Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu Met Met	
	370 375 380	
55	CGC GAG GCG CAG ATC ATG CAC CAG CTG GAC AAC CCC TAC ATC GTG CGG	1200
	Arg Glu Ala Gln Ile Met His Gln Leu Asp Asn Pro Tyr Ile Val Arg	
	385 390 395 400	
60	CTC ATT GGC GTC TGC CAG GCC GAG GCC CTC ATG CTG GTC ATG GAG ATG	1248
	Leu Ile Gly Val Cys Gln Ala Glu Ala Leu Met Leu Val Met Glu Met	
	405 410 415	
65	ATC CCT GTG AGC AAT GTG GCC GAG CTG CTG CAC CAG GTG TCC ATG GGG	1344
	Ile Pro Val Ser Asn Val Ala Glu Leu Leu His Gln Val Ser Met Gly	
	435 440 445	

201

5	ATG AAG TAC CTG GAG GAG AAG AAC TTT GTG CAC CGT GAC CTG GCG GCC	1392
	Met Lys Tyr Leu Glu Glu Lys Asn Phe Val His Arg Asp Leu Ala Ala	
	450 455 460	
10	CGC AAC GTC CTG CTG GTT AAC CGG CAC TAC GCC AAG ATC AGC GAC TTT	1440
	Arg Asn Val Leu Leu Val Asn Arg His Tyr Ala Lys Ile Ser Asp Phe	
	465 470 475 480	
15	GGC CTC TCC AAA GCA CTG GGT GCC GAC GAC AGC TAC TAC ACT GCC CGC	1488
	Gly Leu Ser Lys Ala Leu Gly Ala Asp Asp Ser Tyr Tyr Thr Ala Arg	
	485 490 495	
20	TCA GCA GGG AAG TGG CCG CTC AAG TGG TAC GCA CCC GAA TGC ATC AAC	1536
	Ser Ala Gly Lys Trp Pro Leu Lys Trp Tyr Ala Pro Glu Cys Ile Asn	
	500 505 510	
25	TTC CGC AAG TTC TCC AGC CGC AGC GAT GTC TGG AGC TAT GGG GTC ACC	1584
	Phe Arg Lys Phe Ser Ser Arg Ser Asp Val Trp Ser Tyr Gly Val Thr	
	515 520 525	
30	ATG TGG GAG GCC TTG TCC TAC GGC CAG AAG CCC TAC AAG AAG ATG AAA	1632
	Met Trp Glu Ala Leu Ser Tyr Gly Gln Lys Pro Tyr Lys Lys Met Lys	
	530 535 540	
35	GGG CCG GAG GTC ATG GCC TTC ATC GAG CAG GGC AAG CGG ATG GAG TGC	1680
	Gly Pro Glu Val Met Ala Phe Ile Glu Gln Gly Lys Arg Met Glu Cys	
	545 550 555 560	
40	CCA CCA GAG TGT CCA CCC GAA CTG TAC GCA CTC ATG AGT GAC TGC TGG	1728
	Pro Pro Glu Cys Pro Pro Glu Leu Tyr Ala Leu Met Ser Asp Cys Trp	
	565 570 575	
45	ATC TAC AAG TGG GAG GAT CGC CCC GAC TTC CTG ACC GTG GAG CAG CGC	1776
	Ile Tyr Lys Trp Glu Asp Arg Pro Asp Phe Leu Thr Val Glu Gln Arg	
	580 585 590	
50	ATG CGA GCC TGT TAC TAC AGC CTG GCC AGC AAG GTG GAA GGG CCC CCA	1824
	Met Arg Ala Cys Tyr Tyr Ser Leu Ala Ser Lys Val Glu Gly Pro Pro	
	595 600 605	
55	GGC AGC ACA CAG AAG GCT GAG GCT GCC TGT GCC TGG GAT CCA CCG GTC	1872
	Gly Ser Thr Gln Lys Ala Glu Ala Ala Cys Ala Trp Asp Pro Pro Val	
	610 615 620	
60	GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC	1920
	Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro	
	625 630 635 640	
65	TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG	2016
	Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys	
	660 665 670	

202

5	TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG	2064
	Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val	
	675 680 685	
10	ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC	2112
	Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His	
	690 695 700	
15	ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC	2160
	Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val	
	705 710 715 720	
20	CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC	2208
	Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg	
	725 730 735	
25	GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG	2256
	Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu	
	740 745 750	
30	AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG	2304
	Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu	
	755 760 765	
35	GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG	2352
	Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln	
	770 775 780	
40	AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC	2400
	Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp	
	785 790 795 800	
45	GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC	2448
	Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly	
	805 810 815	
50	GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC	2496
	Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser	
	820 825 830	
55	GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG	2544
	Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu	
	835 840 845	
60	GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC	2592
	Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr	
	850 855 860	

55

(2) INFORMATION FOR SEQ ID NO:111:

203

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 865 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:

Met Pro Asp Pro Ala Ala His Leu Pro Phe Phe Tyr Gly Ser Ile Ser
 1 5 10 15
 Arg Ala Glu Ala Glu Glu His Leu Lys Leu Ala Gly Met Ala Asp Gly
 20 25 30
 Leu Phe Leu Leu Arg Gln Cys Leu Arg Ser Leu Gly Gly Tyr Val Leu
 35 40 45
 Ser Leu Val His Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln
 50 55 60
 Leu Asn Gly Thr Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro
 65 70 75 80
 Ala Glu Leu Cys Glu Phe Tyr Ser Arg Asp Pro Asp Gly Leu Pro Cys
 85 90 95
 Asn Leu Arg Lys Pro Cys Asn Arg Pro Ser Gly Leu Glu Pro Gln Pro
 100 105 110
 Gly Val Phe Asp Cys Leu Arg Asp Ala Met Val Arg Asp Tyr Val Arg
 115 120 125
 Gln Thr Trp Lys Leu Glu Gly Glu Ala Leu Glu Gln Ala Ile Ile Ser
 130 135 140
 Gln Ala Pro Gln Val Glu Lys Leu Ile Ala Thr Thr Ala His Glu Arg
 145 150 155 160
 Met Pro Trp Tyr His Ser Ser Leu Thr Arg Glu Glu Ala Glu Arg Lys
 165 170 175
 Leu Tyr Ser Gly Ala Gln Thr Asp Gly Lys Phe Leu Leu Arg Pro Arg
 180 185 190
 Lys Glu Gln Gly Thr Tyr Ala Leu Ser Leu Ile Tyr Gly Lys Thr Val
 195 200 205
 Tyr His Tyr Leu Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro
 210 215 220
 Glu Gly Thr Lys Phe Asp Thr Leu Trp Gln Leu Val Glu Tyr Leu Lys
 225 230 235 240
 Leu Lys Ala Asp Gly Leu Ile Tyr Cys Leu Lys Glu Ala Cys Pro Asn
 245 250 255
 Ser Ser Ala Ser Asn Ala Ser Gly Ala Ala Ala Pro Thr Leu Pro Ala
 260 265 270
 His Pro Ser Thr Leu Thr His Pro Gln Arg Arg Ile Asp Thr Leu Asn
 275 280 285
 Ser Asp Gly Tyr Thr Pro Glu Pro Ala Arg Ile Thr Ser Pro Asn Lys
 290 295 300
 Leu Leu Ile Ala Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val
 310 315 320 325 330 335
 Arg Gln Gly Val Tyr Arg Met Arg Lys Lys Gln Ile Arg Val A

[illegible]

206

	Gln Gly Leu Ala Phe Cys His Ser His Arg Val Leu His Arg Asp Leu	
	115 120 125	
5	AAA CCT CAG AAT CTG CTT ATT AAC ACA GAG GGG GCC ATC AAG CTA GCA Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu Gly Ala Ile Lys Leu Ala	432
	130 135 140	
10	GAC TTT GGA CTA GCC AGA GCT TTT GGA GTC CCT GTT CGT ACT TAC ACC Asp Phe Gly Leu Ala Arg Ala Phe Gly Val Pro Val Arg Thr Tyr Thr	480
	145 150 155 160	
15	CAT GAG GTG GTG ACC CTG TGG TAC CGA GCT CCT GAA ATC CTC CTG GGC His Glu Val Val Thr Leu Trp Tyr Arg Ala Pro Glu Ile Leu Leu Gly	528
	165 170 175	
20	TCG AAA TAT TAT TCC ACA GCT GTG GAC ATC TGG AGC CTG GGC TGC ATC Ser Lys Tyr Tyr Ser Thr Ala Val Asp Ile Trp Ser Leu Gly Cys Ile	576
	180 185 190	
25	TTT GCT GAG ATG GTG ACT CGC CGG GCC CTG TTC CCT GGA GAT TCT GAG Phe Ala Glu Met Val Thr Arg Arg Ala Leu Phe Pro Gly Asp Ser Glu	624
	195 200 205	
30	ATT GAC CAG CTC TTC CGG ATC TTT CGG ACT CTG GGG ACC CCA GAT GAG Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr Leu Gly Thr Pro Asp Glu	672
	210 215 220	
35	GTG GTG TGG CCA GGA GTT ACT TCT ATG CCT GAT TAC AAG CCA AGT TTC Val Val Trp Pro Gly Val Thr Ser Met Pro Asp Tyr Lys Pro Ser Phe	720
	225 230 235 240	
40	CCC AAG TGG GCC CGG CAA GAT TTT AGT AAA GTT GTA CCT CCC CTG GAT Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys Val Val Pro Pro Leu Asp	768
	245 250 255	
45	GAA GAT GGA CGG AGC TTG TTA TCG CAA ATG CTG CAC TAC GAC CCT AAC Glu Asp Gly Arg Ser Leu Leu Ser Gln Met Leu His Tyr Asp Pro Asn	816
	260 265 270	
50	AAG CGG ATT TCG GCC AAG GCA GCC CTG GCT CAC CCT TTC TTC CAG GAT Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala His Pro Phe Phe Gln Asp	864
	275 280 285	
55	GTG ACC AAG CCA GTA CCC CAT CTT CGA CTC TGG GAT CCA CCG GTC GCC Val Thr Lys Pro Val Pro His Leu Arg Leu Trp Asp Pro Pro Val Ala	912
	290 295 300	
60	ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGC GTG GTG GGC ATC Thr Met Val Val Thr Lys Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr	960
	305 310 315 320 325 330 335	
65	GGC GAG GGC GAG GGC GAT GGC ACC TAC GGC ACC GTC ACC GTC ACC GTC Gly Val Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr	1008
	340 345 350 355 360 365 370 375 380 385 390 395	

207

	Gly	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	
				340					345					350			
5	ATC	TGC	ACC	ACC	GGC	AAG	CTG	CCC	GTG	CCC	TGG	CCC	ACC	CTC	GTG	ACC	1104
	Ile	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	
			355				360					365					
10	ACC	CTG	ACC	TAC	GGC	GTG	CAG	TGC	TTC	AGC	CGC	TAC	CCC	GAC	CAC	ATG	1152
	Thr	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	
		370					375					380					
15	AAG	CAG	CAC	GAC	TTC	TTC	AAG	TCC	GCC	ATG	CCC	GAA	GGC	TAC	GTC	CAG	1200
	Lys	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	
	385					390					395					400	
	GAG	CGC	ACC	ATC	TTC	TTC	AAG	GAC	GAC	GGC	AAC	TAC	AAG	ACC	CGC	GCC	1248
	Glu	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	
				405						410					415		
20	GAG	GTG	AAG	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	CGC	ATC	GAG	CTG	AAG	1296
	Glu	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	
				420				425					430				
25	GGC	ATC	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	CAC	AAG	CTG	GAG	1344
	Gly	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	
		435					440					445					
30	TAC	AAC	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	GAC	AAG	CAG	AAG	1392
	Tyr	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	
		450					455					460					
35	AAC	GGC	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	ATC	GAG	GAC	GGC	1440
	Asn	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	
	465					470				475				480			
	AGC	GTG	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	CCC	ATC	GGC	GAC	1488
	Ser	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	
				485					490					495			
40	GGC	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	ACC	CAG	TCC	GCC	1536
	Gly	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	
				500				505						510			
45	CTG	AGC	AAA	GAC	CCC	AAC	GAG	AAG	CGC	GAT	CAC	ATG	GTC	CTG	CTG	GAG	1584
	Leu	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	
			515				520						525				
	TTC	GTG	ACC	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	GAG	CTG	TAC	AAG	1632
	Thr	Val	Thr	Ala	Ala	Gly	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Thr	

(2) INFORMATION FOR SEQ ID NO:113:

55

(1) SEQUENCE CHARACTERISTICS:

208

(A) LENGTH: 544 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

5

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEO ID NO:113;

10

[illegible]

209

Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met
 370 375 380
 Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln
 385 390 395 400
 5 Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala
 405 410 415
 Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys
 420 425 430
 Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu
 10 435 440 445
 Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys
 450 455 460
 Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly
 465 470 475 480
 15 Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp
 485 490 495
 Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala
 500 505 510
 Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu
 20 515 520 525
 Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
 530 535 540

(2) INFORMATION FOR SEQ ID NO:114:

25

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1635 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

30

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

35

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...1632

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:114:

40

ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG 48
 Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1 5 10 15

45

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC 96
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
 20 25 30

GAG GGC GAG GGC GAT GAT

55

Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr 192
 50 55 60

210

	CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG	240
	Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys	
	65 70 75 80	
5	CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG	288
	Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu	
	85 90 95	
10	CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG	336
	Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu	
	100 105 110	
15	GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC	394
	Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly	
	115 120 125	
20	ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC	432
	Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr	
	130 135 140	
25	AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC	480
	Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn	
	145 150 155 160	
30	GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC	528
	Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser	
	165 170 175	
35	GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC	576
	Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly	
	180 185 190	
40	CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG	624
	Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu	
	195 200 205	
45	AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC	672
	Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe	
	210 215 220	
50	GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC	720
	Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser	
	225 230 235 240	
55	GGA CTC AGA TCT CGA GCC ATG GAG AAC TTC CAA AAG GTG GAA AAG ATC	768
	Gly Leu Arg Ser Arg Ala Met Glu Asn Phe Gln Lys Val Glu Lys Ile	
	245 250 255	
60	GAG AAA GAG GAG GGC TTC AAG AAA ATC CGC CTG GAC ACT GAG ACT GAG	864
	Gly Glu Val Val Ala Leu Lys Lys Ile Arg Leu Asp Thr Glu Thr Glu	
	275 280 285	

211

	GGT GTG CCC AGT ACT GCC ATC CGA GAG ATC TCT CTG CTT AAG GAG CTT	912
	Gly Val Pro Ser Thr Ala Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu	
	290 295 300	
5	AAC CAT CCT AAT ATT GTC AAG CTG CTG GAT GTC ATT CAC ACA GAA AAT	960
	Asn His Pro Asn Ile Val Lys Leu Leu Asp Val Ile His Thr Glu Asn	
	305 310 315 320	
10	AAA CTC TAC CTG GTT TTT GAA TTT CTG CAC CAA GAT CTC AAG AAA TTC	1008
	Lys Leu Tyr Leu Val Phe Glu Phe Leu His Gln Asp Leu Lys Lys Phe	
	325 330 335	
15	ATG GAT GCC TCT GCT CTC ACT GGC ATT CCT CTT CCC CTC ATC AAG AGC	1056
	Met Asp Ala Ser Ala Leu Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser	
	340 345 350	
20	TAT CTG TTC CAG CTG CTC CAG GGC CTA GCT TTC TGC CAT TCT CAT CGG	1104
	Tyr Leu Phe Gln Leu Leu Gln Gly Leu Ala Phe Cys His Ser His Arg	
	355 360 365	
25	GTC CTC CAC CGA GAC CTT AAA CCT CAG AAT CTG CTT ATT AAC ACA GAG	1152
	Val Leu His Arg Asp Leu Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu	
	370 375 380	
30	GGG GCC ATC AAG CTA GCA GAC TTT GGA CTA GCC AGA GCT TTT GGA GTC	1200
	Gly Ala Ile Lys Leu Ala Asp Phe Gly Leu Ala Arg Ala Phe Gly Val	
	385 390 395 400	
35	CCT GTT CGT ACT TAC ACC CAT GAG GTG GTG ACC CTG TGG TAC CGA GCT	1248
	Pro Val Arg Thr Tyr Thr His Glu Val Val Thr Leu Trp Tyr Arg Ala	
	405 410 415	
40	CCT GAA ATC CTC CTG GGC TCG AAA TAT TAT TCC ACA GCT GTG GAC ATC	1296
	Pro Glu Ile Leu Leu Gly Ser Lys Tyr Ser Thr Ala Val Asp Ile	
	420 425 430	
45	TGG AGC CTG GGC TGC ATC TTT GCT GAG ATG GTG ACT CGC CGG GCC CTG	1344
	Trp Ser Leu Gly Cys Ile Phe Ala Glu Met Val Thr Arg Arg Ala Leu	
	435 440 445	
50	TTC CCT GGA GAT TCT GAG ATT GAC CAG CTC TTC CGG ATC TTT CGG ACT	1392
	Phe Pro Gly Asp Ser Glu Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr	
	450 455 460	
55	CTG GGG ACC CCA GAT GAG GTG GTG TGG CCA GGA GTT ACT TCT ATG CCT	1440
	Leu Gly Thr Pro Asp Glu Val Val Trp Pro Gly Val Thr Ser Met Pro	
	465 470 475 480	
60	GAT TTT AAA GGT GAT GAT GAA GAT GGA GGC AGC TTG TTA TCG CAA ATG	1536
	Val Val Pro Pro Leu Asp Glu Asp Gly Arg Ser Leu Leu Ser Gln Met	
	500 505 510	

212

CTG CAC TAC GAC CCT AAC AAG CGG ATT TCG GCC AAG GCA GCC CTG GCT 1584
 Leu His Tyr Asp Pro Asn Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala
 515 520 525

5 CAC CCT TTC TTC CAG GAT GTG ACC AAG CCA GTA CCC CAT CTT CGA CTC T 1633
 His Pro Phe Phe Gln Asp Val Thr Lys Pro Val Pro His Leu Arg Leu
 530 535 540

GA 1635

(2) INFORMATION FOR SEQ ID NO:115:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 544 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:115:

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1 5 10 15
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
 20 25 30
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
 35 40 45
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 50 55 60
 Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
 65 70 75 80
 Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
 85 90 95
 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
 100 105 110
 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
 115 120 125
 Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
 130 135 140
 Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
 145 150 155 160
 Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
 165 170 175
 Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
 180 185 190
 Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu

220 230 235 240
 Gly Leu Arg Ser Arg Ala Met Glu Asn Phe Gln Lys Val Glu Lys Ile
 245 250 255
 Gly Glu Gly Thr Tyr Gly Val Val Tyr Lys Ala Arg Asn Lys Leu Thr

213

[illegible]

(2) INFORMATION FOR SEQ ID NO:116:

(i) SEQUENCE CHARACTERISTICS:

40 (A) LENGTH: 2532 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

(A) NAME/KEY: Coding Sequence

(B) LOCATION: [REDACTED]

55 ATG GTC AGC AAG GGC GAG GAG CTC TTC ACC GGG GTG GTG CCC ATC CTC
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1 5 10 15

43

214

	GTC	GAG	CTG	GAC	GGC	GAC	GTA	AAC	GGC	CAC	AAG	TTC	AGC	GTG	TCC	GGC	96
	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	
				20					25					30			
5	GAG	GGC	GAG	GGC	GAT	GCC	ACC	TAC	GGC	AAG	CTG	ACC	CTG	AAG	TTC	ATC	144
	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	
			35					40					45				
10	TGC	ACC	ACC	GGC	AAG	CTG	CCC	GTG	CCC	TGG	CCC	ACC	CTC	GTG	ACC	ACC	192
	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	
		50					55					60					
15	CTG	ACC	TAC	GGC	GTG	CAG	TGC	TTC	AGC	CGC	TAC	CCC	GAC	CAC	ATG	AAG	240
	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	
	65					70				75						80	
20	CAG	CAC	GAC	TTC	TTC	AAG	TCC	GCC	ATG	CCC	GAA	GGC	TAC	GTC	CAG	GAG	288
	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	
					85					90					95		
25	CGC	ACC	ATC	TTC	TTC	AAG	GAC	GAC	GGC	AAC	TAC	AAG	ACC	CGC	GCC	GAG	336
	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	
				100					105					110			
30	GTG	AAG	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	CGC	ATC	GAG	CTG	AAG	GGC	384
	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	
			115					120					125				
35	ATC	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	CAC	AAG	CTG	GAG	TAC	432
	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	
		130					135					140					
40	AAC	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	GAC	AAG	CAG	AAG	AAC	480
	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	
		145				150					155					160	
45	GGC	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	ATC	GAG	GAC	GGC	AGC	528
	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	
					165				170						175		
50	GTG	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	CCC	ATC	GGC	GAC	GGC	576
	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	
				180				185					190				
55	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	ACC	CAG	TCC	GCC	CTG	624
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	
			195					200					205				
60	GTG	ACC	GGC	GGC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	GAG	CTG	TAC	AAG	TCC	720
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser	
		225				230					235						

215

5	GGA	CTC	AGA	TCT	CGA	GAG	ATG	CTG	TCC	CGT	GGG	TGG	TTT	CAC	CGA	GAC	768
	Gly	Leu	Arg	Ser	Arg	Glu	Met	Leu	Ser	Arg	Gly	Trp	Phe	His	Arg	Asp	
	245				250				255								
10	CTC	AGT	GGG	CTG	GAT	GCA	GAG	ACC	CTG	CTC	AAG	GGC	CGA	GGT	GTC	CAC	816
	Leu	Ser	Gly	Leu	Asp	Ala	Glu	Thr	Leu	Leu	Lys	Gly	Arg	Gly	Val	His	
	260				265				270								
15	GGT	AGC	TTC	CTG	GCT	CGG	CCC	AGT	CGC	AAG	AAC	CAG	GGT	GAC	TTC	TCG	864
	Gly	Ser	Phe	Leu	Ala	Arg	Pro	Ser	Arg	Lys	Asn	Gln	Gly	Asp	Phe	Ser	
	275				280				285								
20	CTC	TCC	GTC	AGG	GTG	GGC	GAT	CAG	GTG	ACC	CAT	ATT	CGG	ATC	CAG	AAC	912
	Leu	Ser	Val	Arg	Val	Gly	Asp	Gln	Val	Thr	His	Ile	Arg	Ile	Gln	Asn	
	290				295				300								
25	TCA	GGG	GAT	TTC	TAT	GAC	CTG	TAT	GGA	GGG	GAG	AAG	TTT	GCG	ACT	CTG	960
	Ser	Gly	Asp	Phe	Tyr	Asp	Leu	Tyr	Gly	Gly	Glu	Lys	Phe	Ala	Thr	Leu	
	305				310				315				320				
30	ACA	GAG	CTG	GTG	GAG	TAC	TAC	ACT	CAG	CAG	CAG	GGT	GTC	CTG	CAG	GAC	1008
	Thr	Glu	Leu	Val	Glu	Tyr	Tyr	Thr	Gln	Gln	Gln	Gly	Val	Leu	Gln	Asp	
	325				330				335								
35	CGC	GAC	GGC	ACC	ATC	ATC	CAC	CTC	AAG	TAC	CCG	CTG	AAC	TGC	TCC	GAT	1056
	Arg	Asp	Gly	Thr	Ile	Ile	His	Leu	Lys	Tyr	Pro	Leu	Asn	Cys	Ser	Asp	
	340				345				350								
40	CCC	ACT	AGT	GAG	AGG	TGG	TAC	CAT	GGC	CAC	ATG	TCT	GGC	GGG	CAG	GCA	1104
	Pro	Thr	Ser	Glu	Arg	Trp	Tyr	His	Gly	His	Met	Ser	Gly	Gly	Gln	Ala	
	355				360				365								
45	GAG	ACG	CTG	CTG	CAG	GCC	AAG	GGC	GAG	CCC	TGG	ACG	TTT	CTT	GTG	CGT	1152
	Glu	Thr	Leu	Leu	Gln	Ala	Lys	Gly	Glu	Pro	Trp	Thr	Phe	Leu	Val	Arg	
	370				375				380								
50	GAG	AGC	CTC	AGC	CAG	CCT	GGA	GAC	TTC	GTG	CTT	TCT	GTG	CTC	AGT	GAC	1200
	Glu	Ser	Leu	Ser	Gln	Pro	Gly	Asp	Phe	Val	Leu	Ser	Val	Leu	Ser	Asp	
	385				390				395				400				
55	CAG	CCC	AAG	GCT	GGC	CCA	GGC	TCC	CCG	CTC	AGG	GTC	ACC	CAC	ATC	AAG	1248
	Gln	Pro	Lys	Ala	Gly	Pro	Gly	Ser	Pro	Leu	Arg	Val	Thr	His	Ile	Lys	
	405				410				415								
60	GTC	ATG	TGC	GAG	GGT	GGA	CGC	TAC	ACA	GTG	GGT	GGT	TTG	GAG	ACC	TTC	1296
	Val	Met	Cys	Glu	Gly	Gly	Arg	Tyr	Thr	Val	Gly	Gly	Leu	Glu	Thr	Phe	
	420				425				430								
65	GAG	GCC	TCA	GGC	GCC	TTT	GTC	TAC	CTG	CGG	CAG	CCG	TAC	TAT	GCC	ACG	1392
	Glu	Ala	Ser	Gly	Ala	Phe	Val	Tyr	Leu	Arg	Gln	Pro	Tyr	Tyr	Ala	Thr	
	450				455				460								

216

5	AGG GTG AAT GCG GCT GAC ATT GAG AAC CGA GTG TTG GAA CTG AAC AAG	1440
	Arg Val Asn Ala Ala Asp Ile Glu Asn Arg Val Leu Glu Leu Asn Lys	
	465 470 475 480	
10	AAG CAG GAG TCC GAG GAT ACA GCC AAG GCT GGC TTC TGG GAG GAG TTT	1488
	Lys Gln Glu Ser Glu Asp Thr Ala Lys Ala Gly Phe Trp Glu Glu Phe	
	485 490 495	
15	GAG AGT TTG CAG AAG CAG GAG GTG AAG AAC TTG CAC CAG CGT CTG GAA	1536
	Glu Ser Leu Gln Lys Gln Glu Val Lys Asn Leu His Gln Arg Leu Glu	
	500 505 510	
20	GGG CAG CGG CCA GAG AAC AAG GGC AAG AAC CGC TAC AAG AAC ATT CTC	1584
	Gly Gln Arg Pro Glu Asn Lys Gly Lys Asn Arg Tyr Lys Asn Ile Leu	
	515 520 525	
25	CCC TTT GAC CAC AGC CGA GTG ATC CTG CAG GGA CGG GAC AGT AAC ATC	1632
	Pro Phe Asp His Ser Arg Val Ile Leu Gln Gly Arg Asp Ser Asn Ile	
	530 535 540	
30	CCC GGG TCC GAC TAC ATC AAT GCC AAC TAC ATC AAG AAC CAG CTG CTA	1680
	Pro Gly Ser Asp Tyr Ile Asn Ala Asn Tyr Ile Lys Asn Gln Leu Leu	
	545 550 555 560	
35	GGC CCT GAT GAG AAC GCT AAG ACC TAC ATC GCC AGC CAG GGC TGT CTG	1728
	Gly Pro Asp Glu Asn Ala Lys Thr Tyr Ile Ala Ser Gln Gly Cys Leu	
	565 570 575	
40	GAG GCC ACG GTC AAT GAC TTC TGG CAG ATG GCG TGG CAG GAG AAC AGC	1776
	Glu Ala Thr Val Asn Asp Phe Trp Gln Met Ala Trp Gln Glu Asn Ser	
	580 585 590	
45	CGT GTC ATC GTC ATG ACC ACC CGA GAG GTG GAG AAA GGC CGG AAC AAA	1824
	Arg Val Ile Val Met Thr Thr Arg Glu Val Glu Lys Gly Arg Asn Lys	
	595 600 605	
50	TGC GTC CCA TAC TGG CCC GAG GTG GGC ATG CAG CGT GCT TAT GGG CCC	1872
	Cys Val Pro Tyr Trp Pro Glu Val Gly Met Gln Arg Ala Tyr Gly Pro	
	610 615 620	
55	TAC TCT GTG ACC AAC TGC GGG GAG CAT GAC ACA ACC GAA TAC AAA CTC	1920
	Tyr Ser Val Thr Asn Cys Gly Glu His Asp Thr Thr Glu Tyr Lys Leu	
	625 630 635 640	
60	CGT ACC TTA CAG GTC TCC CCG CTG GAC AAT GGA GAC CTG ATT CGG GAG	1968
	Arg Thr Leu Gln Val Ser Pro Leu Asp Asn Gly Asp Leu Ile Arg Glu	
	645 650 655	
65	GAG CCT GGG GGT GTC CTC AGC TTC CTG GAC CAG ATC AAC CAG CGG CAG	2064
	Glu Pro Gly Gly Val Leu Ser Phe Leu Asp Gln Ile Asn Gln Arg Gln	
	675 680 685	

217

5	GAA AGT CTG CCT CAC GCA GGG CCC ATC ATC GTG CAC TGC AGC GCC GGC	2112
	Glu Ser Leu Pro His Ala Gly Pro Ile Ile Val His Cys Ser Ala Gly	
	690 695 700	
10	ATC GGC CGC ACA GGC ACC ATC ATT GTC ATC GAC ATG CTC ATG GAG AAC	2160
	Ile Gly Arg Thr Gly Thr Ile Ile Val Ile Asp Met Leu Met Glu Asn	
	705 710 715 720	
15	ATC TCC ACC AAG GGC CTG GAC TGT GAC ATT GAC ATC CAG AAG ACC ATC	2208
	Ile Ser Thr Lys Gly Leu Asp Cys Asp Ile Asp Ile Gln Lys Thr Ile	
	725 730 735	
20	CAG ATG GTG CGG GCG CAG CGC TCG GGC ATG GTG CAG ACG GAG GCG CAG	2256
	Gln Met Val Arg Ala Gln Arg Ser Gly Met Val Gln Thr Glu Ala Gln	
	740 745 750	
25	TAC AAG TTC ATC TAC GTG GCC ATC GCC CAG TTC ATT GAA ACC ACT AAG	2304
	Tyr Lys Phe Ile Tyr Val Ala Ile Ala Gln Phe Ile Glu Thr Thr Lys	
	755 760 765	
30	AAG AAG CTG GAG GTC CTG CAG TCG CAG AAG GGC CAG GAG TCG GAG TAC	2352
	Lys Lys Leu Glu Val Leu Gln Ser Gln Lys Gly Gln Glu Ser Glu Tyr	
	770 775 780	
35	GGG AAC ATC ACC TAT CCC CCA GCC ATG AAG AAT GCC CAT GCC AAG GCC	2400
	Gly Asn Ile Thr Tyr Pro Pro Ala Met Lys Asn Ala His Ala Lys Ala	
	785 790 795 800	
40	TCC CGC ACC TCG TCC AAA CAC AAG GAG GAT GTG TAT GAG AAC CTG CAC	2448
	Ser Arg Thr Ser Ser Lys His Lys Glu Asp Val Tyr Glu Asn Leu His	
	805 810 815	
45	ACT AAG AAC AAG AGG GAG GAG AAA GTG AAG AAG CAG CGG TCA GCA GAC	2496
	Thr Lys Asn Lys Arg Glu Glu Lys Val Lys Lys Gln Arg Ser Ala Asp	
	820 825 830	
50	AAG GAG AAG AGC AAG GGT TCC CTC AAG AGG AAG TGA	2532
	Lys Glu Lys Ser Lys Gly Ser Leu Lys Arg Lys	
	835 840	

(2) INFORMATION FOR SEQ ID NO:117:

- 45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 843 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single

SEQUENCE DESCRIPTION:

- 55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:117:

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Glu Val Val ...

[illegible]

Val	Met	Cys	Glu	Gly	Gly	Arg	Tyr	Thr	Val	Gly	Gly	Leu	Glu	Thr	Ile
			420					425					430		
Asp	Ser	Leu	Thr	Asp	Leu	Val	Glu	His	Phe	Lys	Lys	Thr	Gly	Ile	Glu
								435					445		

219

[illegible]

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2562 base pairs

(B) TYPE: nucleic acid

Table 1. Demographic characteristics of the study population

220

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

5

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...2559

(D) OTHER INFORMATION:

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:118:

ATG CTG TCC CGT GGG TGG TTT CAC CGA GAC CTC AGT GGG CTG GAT GCA	48
Met Leu Ser Arg Gly Trp Phe His Arg Asp Leu Ser Gly Leu Asp Ala	
1 5 10 15	
GAG ACC CTG CTC AAG GGC CGA GGT GTC CAC GGT AGC TTC CTG GCT CGG	96
Glu Thr Leu Leu Lys Gly Arg Gly Val His Gly Ser Phe Leu Ala Arg	
20 25 30	
CCC AGT CGC AAG AAC CAG GGT GAC TTC TCG CTC TCC GTC AGG GTG GGG	144
Pro Ser Arg Lys Asn Gln Gly Asp Phe Ser Leu Ser Val Arg Val Gly	
35 40 45	
GAT CAG GTG ACC CAT ATT CGG ATC CAG AAC TCA GGG GAT TTC TAT GAC	192
Asp Gln Val Thr His Ile Arg Ile Gln Asn Ser Gly Asp Phe Tyr Asp	
50 55 60	
CTG TAT GGA GGG GAG AAG TTT GCG ACT CTG ACA GAG CTG GTG GAG TAC	240
Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu Thr Glu Leu Val Glu Tyr	
65 70 75 80	
TAC ACT CAG CAG CAG GGT GTC CTG CAG GAC CGC GAC GGC ACC ATC ATC	288
Tyr Thr Gln Gln Gln Gly Val Leu Gln Asp Arg Asp Gly Thr Ile Ile	
85 90 95	
CAC CTC AAG TAC CCG CTG AAC TGC TCC GAT CCC ACT AGT GAG AGG TGG	336
His Leu Lys Tyr Pro Leu Asn Cys Ser Asp Pro Thr Ser Glu Arg Trp	
100 105 110	
TAC CAT GGC CAC ATG TCT GGC GGG CAG GCA GAG ACG CTG CTG CAG GCC	384
Tyr His Gly His Met Ser Gly Gly Gln Ala Glu Thr Leu Leu Gln Ala	
115 120 125	
AAG GGC GAG CCC TGG ACG TTT CTT GTG CGT GAG AGC CTC AGC CAG CCT	432
Lys Gly Glu Pro Trp Thr Phe Leu Val Arg Glu Ser Leu Ser Gln Pro	
130 135 140	
GGA GAC TTC GTG CTT TCT GTG CTC AGT GAC CAG CCC AAG GGT GGC GCA	
Gly Ser Pro Leu Arg Val Thr His Ile Lys Val Met Cys Glu Gly Gly	
165 170 175	
CGC TAC ACA GTG GGT GGT TTT GAG TGG TGG GAG GAG GAG GAG	

55

221

	Arg	Tyr	Thr	Val	Gly	Gly	Leu	Glu	Thr	Phe	Asp	Ser	Leu	Thr	Asp	Leu	
				180					185					190			
5	GTA	GAG	CAT	TTC	AAG	AAG	ACG	GGG	ATT	GAG	GAG	GCC	TCA	GGC	GCC	TTT	624
	Val	Glu	His	Phe	Lys	Lys	Thr	Gly	Ile	Glu	Glu	Ala	Ser	Gly	Ala	Phe	
			195					200					205				
10	GTC	TAC	CTG	CGG	CAG	CCG	TAC	TAT	GCC	ACG	AGG	GTG	AAT	GCG	GCT	GAC	672
	Val	Tyr	Leu	Arg	Gln	Pro	Tyr	Tyr	Ala	Thr	Arg	Val	Asn	Ala	Ala	Asp	
		210					215					220					
15	ATT	GAG	AAC	CGA	GTG	TTG	GAA	CTG	AAC	AAG	AAG	CAG	GAG	TCC	GAG	GAT	720
	Ile	Glu	Asn	Arg	Val	Leu	Glu	Leu	Asn	Lys	Lys	Gln	Glu	Ser	Glu	Asp	
	225					230					235				240		
	ACA	GCC	AAG	GCT	GGC	TTC	TGG	GAG	GAG	TTT	GAG	AGT	TTG	CAG	AAG	CAG	768
	Thr	Ala	Lys	Ala	Gly	Phe	Trp	Glu	Glu	Phe	Glu	Ser	Leu	Gln	Lys	Gln	
				245					250					255			
20	GAG	GTG	AAG	AAC	TTG	CAC	CAG	CGT	CTG	GAA	GGG	CAG	CGG	CCA	GAG	AAC	816
	Glu	Val	Lys	Asn	Leu	His	Gln	Arg	Leu	Glu	Gly	Gln	Arg	Pro	Glu	Asn	
			260					265					270				
25	AAG	GGC	AAG	AAC	CGC	TAC	AAG	AAC	ATT	CTC	CCC	TTT	GAC	CAC	AGC	CGA	864
	Lys	Gly	Lys	Asn	Arg	Tyr	Lys	Asn	Ile	Leu	Pro	Phe	Asp	His	Ser	Arg	
		275					280						285				
30	GTG	ATC	CTG	CAG	GGA	CGG	GAC	AGT	AAC	ATC	CCC	GGG	TCC	GAC	TAC	ATC	912
	Val	Ile	Leu	Gln	Gly	Arg	Asp	Ser	Asn	Ile	Pro	Gly	Ser	Asp	Tyr	Ile	
		290				295					300						
35	AAT	GCC	AAC	TAC	ATC	AAG	AAC	CAG	CTG	CTA	GGC	CCT	GAT	GAG	AAC	GCT	960
	Asn	Ala	Asn	Tyr	Ile	Lys	Asn	Gln	Leu	Leu	Gly	Pro	Asp	Glu	Asn	Ala	
	305					310					315				320		
	AAG	ACC	TAC	ATC	GCC	AGC	CAG	GGC	TGT	CTG	GAG	GCC	ACG	GTC	AAT	GAC	1008
	Lys	Thr	Tyr	Ile	Ala	Ser	Gln	Gly	Cys	Leu	Glu	Ala	Thr	Val	Asn	Asp	
				325				330						335			
40	TTC	TGG	CAG	ATG	GCG	TGG	CAG	GAG	AAC	AGC	CGT	GTC	ATC	GTC	ATG	ACC	1056
	Phe	Trp	Gln	Met	Ala	Trp	Gln	Glu	Asn	Ser	Arg	Val	Ile	Val	Met	Thr	
			340					345					350				
45	ACC	CGA	GAG	GTG	GAG	AAA	GGC	CGG	AAC	AAA	TGC	GTC	CCA	TAC	TGG	CCC	1104
	Thr	Arg	Glu	Val	Glu	Lys	Gly	Arg	Asn	Lys	Cys	Val	Pro	Tyr	Trp	Pro	
		355					360					365					
55	GAG	GTG	GGC	ATG	CAG	CGT	GCT	TAT	GGG	GGC	TAG	TCT	GTC	AGC	AAG	TCC	1152
	Gly	Glu	His	Asp	Thr	Thr	Glu	Tyr	Lys	Leu	Arg	Thr	Leu	Gln	Val	Ser	
	385					390					395				400		
	GGG	GTG	GAG	ATG	CAG	CGT	GCT	TAT	GGG	GGC	TAG	TCT	GTC	AGC	AAG	TCC	

222

	Pro	Leu	Asp	Asn	Gly	Asp	Leu	Ile	Arg	Glu	Ile	Trp	His	Tyr	Gln	Tyr	
					405					410					415		
5	CTG	AGC	TGG	CCC	GAC	CAT	GGG	GTC	CCC	AGT	GAG	CCT	GGG	GGT	GTC	CTC	1296
	Leu	Ser	Trp	Pro	Asp	His	Gly	Val	Pro	Ser	Glu	Pro	Gly	Gly	Val	Leu	
				420					425					430			
10	AGC	TTC	CTG	GAC	CAG	ATC	AAC	CAG	CGG	CAG	GAA	AGT	CTG	CCT	CAC	GCA	1344
	Ser	Phe	Leu	Asp	Gln	Ile	Asn	Gln	Arg	Gln	Glu	Ser	Leu	Pro	His	Ala	
			435					440					445				
15	GGG	CCC	ATC	ATC	GTG	CAC	TGC	AGC	GCC	GGC	ATC	GGC	CGC	ACA	GGC	ACC	1392
	Gly	Pro	Ile	Ile	Val	His	Cys	Ser	Ala	Gly	Ile	Gly	Arg	Thr	Gly	Thr	
		450					455					460					
20	ATC	ATT	GTC	ATC	GAC	ATG	CTC	ATG	GAG	AAC	ATC	TCC	ACC	AAG	GGC	CTG	1440
	Ile	Ile	Val	Ile	Asp	Met	Leu	Met	Glu	Asn	Ile	Ser	Thr	Lys	Gly	Leu	
	465					470					475				480		
25	GAC	TGT	GAC	ATT	GAC	ATC	CAG	AAG	ACC	ATC	CAG	ATG	GTG	CGG	GCG	CAG	1488
	Asp	Cys	Asp	Ile	Asp	Ile	Gln	Lys	Thr	Ile	Gln	Met	Val	Arg	Ala	Gln	
					485					490					495		
30	CGC	TCG	GGC	ATG	GTG	CAG	ACG	GAG	GCG	CAG	TAC	AAG	TTC	ATC	TAC	GTG	1536
	Arg	Ser	Gly	Met	Val	Gln	Thr	Glu	Ala	Gln	Tyr	Lys	Phe	Ile	Tyr	Val	
			500						505					510			
35	GCC	ATC	GCC	CAG	TTC	ATT	GAA	ACC	ACT	AAG	AAG	AAG	CTG	GAG	GTC	CTG	1584
	Ala	Ile	Ala	Gln	Phe	Ile	Glu	Thr	Thr	Lys	Lys	Lys	Leu	Glu	Val	Leu	
			515					520					525				
40	CAG	TCG	CAG	AAG	GGC	CAG	GAG	TCG	GAG	TAC	GGG	AAC	ATC	ACC	TAT	CCC	1632
	Gln	Ser	Gln	Lys	Gly	Gln	Glu	Ser	Glu	Tyr	Gly	Asn	Ile	Thr	Tyr	Pro	
		530					535					540					
45	CCA	GCC	ATG	AAG	AAT	GCC	CAT	GCC	AAG	GCC	TCC	CGC	ACC	TCG	TCC	AAA	1680
	Pro	Ala	Met	Lys	Asn	Ala	His	Ala	Lys	Ala	Ser	Arg	Thr	Ser	Ser	Lys	
		545				550					555					560	
50	CAC	AAG	GAG	GAT	GTG	TAT	GAG	AAC	CTG	CAC	ACT	AAG	AAC	AAG	AGG	GAG	1728
	His	Lys	Glu	Asp	Val	Tyr	Glu	Asn	Leu	His	Thr	Lys	Asn	Lys	Arg	Glu	
					565					570					575		
55	GAG	AAA	GTG	AAG	AAG	CAG	CGG	TCA	GCA	GAC	AAG	GAG	AAG	AGC	AAG	GGT	1776
	Glu	Lys	Val	Lys	Lys	Gln	Arg	Ser	Ala	Asp	Lys	Glu	Lys	Ser	Lys	Gly	
			580						585					590			
	TCG	CTG	AAG	AGG	AAG	GGA	ACT	CTG	GAG	TCG	AAG	GGT	GGG	GGG	GGG	GGG	1824
	Asp	Pro	Pro	Val	Ala	Thr	Met	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	
		610						615					620				

223

	Gly	Val	Val	Pro	Ile	Leu	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	
	625					630					635					640	
5	AAG	TTC	AGC	GTG	TCC	GGC	GAG	GGC	GAG	GGC	GAT	GCC	ACC	TAC	GGC	AAG	1968
	Lys	Phe	Ser	Val	Ser	Gly	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	
					645					650					655		
10	CTG	ACC	CTG	AAG	TTC	ATC	TGC	ACC	ACC	GGC	AAG	CTG	CCC	GTG	CCC	TGG	2016
	Leu	Thr	Leu	Lys	Phe	Ile	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	
				660						665				670			
15	CCC	ACC	CTC	GTG	ACC	ACC	CTG	ACC	TAC	GGC	GTG	CAG	TGC	TTC	AGC	CGC	2064
	Pro	Thr	Leu	Val	Thr	Thr	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	
			675					680					685				
	TAC	CCC	GAC	CAC	ATG	AAG	CAG	CAC	GAC	TTC	TTC	AAG	TCC	GCC	ATG	CCC	2112
	Tyr	Pro	Asp	His	Met	Lys	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	
		690					695					700					
20	GAA	GGC	TAC	GTC	CAG	GAG	CGC	ACC	ATC	TTC	TTC	AAG	GAC	GAC	GGC	AAC	2160
	Glu	Gly	Tyr	Val	Gln	Glu	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	
	705					710					715				720		
25	TAC	AAG	ACC	CGC	GCC	GAG	GTG	AAG	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	2208
	Tyr	Lys	Thr	Arg	Ala	Glu	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	
				725						730				735			
30	CGC	ATC	GAG	CTG	AAG	GGC	ATC	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	2256
	Arg	Ile	Glu	Leu	Lys	Gly	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	
			740						745					750			
35	GGG	CAC	AAG	CTG	GAG	TAC	AAC	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	2304
	Gly	His	Lys	Leu	Glu	Tyr	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	
			755				760						765				
	GCC	GAC	AAG	CAG	AAG	AAC	GGC	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	2352
	Ala	Asp	Lys	Gln	Lys	Asn	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	
		770					775					780					
40	AAC	ATC	GAG	GAC	GGC	AGC	GTG	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	2400
	Asn	Ile	Glu	Asp	Gly	Ser	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	
	785					790					795				800		
45	ACC	CCC	ATC	GGC	GAC	GGC	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	2448
	Thr	Pro	Ile	Gly	Asp	Gly	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	
				805					810					815			
	AGC	ACC	CAG	TCC	GCC	CTG	AGC	AAA	GAC	CCC	AAC	GAG	AAG	CGC	GAT	CAC	2496
55	Met	Val	Leu	Leu	Glu	Phe	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	
			835					840					845				
	GAC	GAG	CTG	TAC	AAG	TAA											

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:

	Met	Leu	Ser	Arg	Gly	Trp	Phe	His	Arg	Asp	Leu	Ser	Gly	Leu	Asp	Ala
	1				5					10					15	
20	Glu	Thr	Leu	Leu	Lys	Gly	Arg	Gly	Val	His	Gly	Ser	Phe	Leu	Ala	Arg
				20					25					30		
	Pro	Ser	Arg	Lys	Asn	Gln	Gly	Asp	Phe	Ser	Leu	Ser	Val	Arg	Val	Gly
			35					40					45			
25	Asp	Gln	Val	Thr	His	Ile	Arg	Ile	Gln	Asn	Ser	Gly	Asp	Phe	Tyr	Asp
	50						55					60				
	Leu	Tyr	Gly	Gly	Glu	Lys	Phe	Ala	Thr	Leu	Thr	Glu	Leu	Val	Glu	Tyr
	65					70					75					80
	Tyr	Thr	Gln	Gln	Gln	Gly	Val	Leu	Gln	Asp	Arg	Asp	Gly	Thr	Ile	Ile
					85					90					95	
30	His	Leu	Lys	Tyr	Pro	Leu	Asn	Cys	Ser	Asp	Pro	Thr	Ser	Glu	Arg	Trp
				100					105					110		
	Tyr	His	Gly	His	Met	Ser	Gly	Gly	Gln	Ala	Glu	Thr	Leu	Leu	Gln	Ala
			115					120					125			
35	Lys	Gly	Glu	Pro	Trp	Thr	Phe	Leu	Val	Arg	Glu	Ser	Leu	Ser	Gln	Pro
	130						135					140				
	Gly	Asp	Phe	Val	Leu	Ser	Val	Leu	Ser	Asp	Gln	Pro	Lys	Ala	Gly	Pro
	145					150					155					160
	Gly	Ser	Pro	Leu	Arg	Val	Thr	His	Ile	Lys	Val	Met	Cys	Glu	Gly	Gly
					165					170					175	
40	Arg	Tyr	Thr	Val	Gly	Gly	Leu	Glu	Thr	Phe	Asp	Ser	Leu	Thr	Asp	Leu
				180					185					190		
	Val	Glu	His	Phe	Lys	Lys	Thr	Gly	Ile	Glu	Glu	Ala	Ser	Gly	Ala	Phe
			195					200					205			
45	Val	Tyr	Leu	Arg	Gln	Pro	Tyr	Tyr	Ala	Thr	Arg	Val	Asn	Ala	Ala	Asp
	210						215					220				
	Ile	Glu	Asn	Arg	Val	Leu	Glu	Leu	Asn	Lys	Lys	Gln	Glu	Ser	Glu	Asp
	225					230					235					240
	Thr	Ala	Lys	Ala	Gly	Phe	Trp	Gly	Gly	Phe	Gly	Ser	Leu	Gly	Lys	Gly

	275		280		285
	Val Ile Leu Gln Gly Arg Asp	Ser Asn Ile Pro Gly Ser Asp Tyr Ile			
55	290		295		300
	Asp His Asp Thr Ile Leu	Asp Thr Thr Thr Thr Thr Thr			

[illegible]

226

755 760 765
 Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His
 770 775 780
 Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn
 5 785 790 795 800
 Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu
 805 810 815
 Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His
 820 825 830
 10 Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met
 835 840 845
 Asp Glu Leu Tyr Lys
 850

15 (2) INFORMATION FOR SEQ ID NO:120:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2994 base pairs

(B) TYPE: nucleic acid

20 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

25

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...2991

(D) OTHER INFORMATION:

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:

ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG 48
 Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1 5 10 15
 35 GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC 96
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
 20 25 30
 40 GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC 144
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
 35 40 45
 45 TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC 192
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 50 55 60
 CTG ACC TAG GGC GTG GAG TGG TGG ACC GGC TAC GGC GAG GAG TGG TGG
 65 70 75
 Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
 85 90 95

55

227

	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	
				100					105						110		
5	GTG	AAG	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	CGC	ATC	GAG	CTG	AAG	GGC	384
	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	
			115					120					125				
10	ATC	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	CAC	AAG	CTG	GAG	TAC	432
	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	
			130				135					140					
15	AAC	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	GAC	AAG	CAG	AAG	AAC	480
	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	
	145					150					155					160	
	GGC	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	ATC	GAG	GAC	GGC	AGC	528
	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	
					165					170					175		
20	GTG	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	CCC	ATC	GGC	GAC	GGC	576
	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	
				180					185					190			
25	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	ACC	CAG	TCC	GCC	CTG	624
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	
			195					200					205				
30	AGC	AAA	GAC	CCC	AAC	GAG	AAG	CGC	GAT	CAC	ATG	GTC	CTG	CTG	GAG	TTC	672
	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	
		210					215					220					
35	GTG	ACC	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	GAG	CTG	TAC	AAG	TCC	720
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser	
	225					230					235					240	
	GGA	CTC	AGA	TCT	CGA	GCT	CAA	GCT	TCG	AAT	TCG	ACC	ATG	GAG	CGG	CCC	768
	Gly	Leu	Arg	Ser	Arg	Ala	Gln	Ala	Ser	Asn	Ser	Thr	Met	Glu	Arg	Pro	
					245					250					255		
40	CCG	GGG	CTG	CGG	CCG	GGC	GCG	GGC	GGG	CCC	TGG	GAG	ATG	CGG	GAG	CGG	816
	Pro	Gly	Leu	Arg	Pro	Gly	Ala	Gly	Gly	Pro	Trp	Glu	Met	Arg	Glu	Arg	
				260					265					270			
45	CTG	GGC	ACC	GGC	GGC	TTC	GGG	AAC	GTC	TGT	CTG	TAC	CAG	CAT	CGG	GAA	864
	Leu	Gly	Thr	Gly	Gly	Phe	Gly	Asn	Val	Cys	Leu	Tyr	Gln	His	Arg	Glu	
			275					280					285				
	CTT	GAT	CTG	AAA	ATA	GCA	ATT	AAG	TGT	TGT	CGG	CTA	GAG	CTA	AGT	ACC	912
55	Lys	Asn	Arg	Glu	Arg	Trp	Cys	His	Glu	Ile	Gln	Ile	Met	Lys	Lys	Leu	
	305					310					315					320	
	AAG	GAT	CGC	AAT	GTT	GCT	AAC	AAA	TGT	GAT	GCT	GCT	GAA	GAT	TCT	AAT	1008

228

	Asn	His	Ala	Asn	Val	Val	Lys	Ala	Cys	Asp	Val	Pro	Glu	Glu	Leu	Asn	
				325						330					335		
5	ATT	TTG	ATT	CAT	GAT	GTG	CCT	CTT	CTA	GCA	ATG	GAA	TAC	TGT	TCT	GGA	1056
	Ile	Leu	Ile	His	Asp	Val	Pro	Leu	Leu	Ala	Met	Glu	Tyr	Cys	Ser	Gly	
				340					345					350			
10	GGA	GAT	CTC	CGA	AAG	CTG	CTC	AAC	AAA	CCA	GAA	AAT	TGT	TGT	GGA	CTT	1104
	Gly	Asp	Leu	Arg	Lys	Leu	Leu	Asn	Lys	Pro	Glu	Asn	Cys	Cys	Gly	Leu	
			355					360					365				
15	AAA	GAA	AGC	CAG	ATA	CTT	TCT	TTA	CTA	AGT	GAT	ATA	GGG	TCT	GGG	ATT	1152
	Lys	Glu	Ser	Gln	Ile	Leu	Ser	Leu	Leu	Ser	Asp	Ile	Gly	Ser	Gly	Ile	
		370					375				380						
20	CGA	TAT	TTG	CAT	GAA	AAC	AAA	ATT	ATA	CAT	CGA	GAT	CTA	AAA	CCT	GAA	1200
	Arg	Tyr	Leu	His	Glu	Asn	Lys	Ile	Ile	His	Arg	Asp	Leu	Lys	Pro	Glu	
	385					390					395					400	
25	AAC	ATA	GTT	CTT	CAG	GAT	GTT	GGT	GGA	AAG	ATA	ATA	CAT	AAA	ATA	ATT	1248
	Asn	Ile	Val	Leu	Gln	Asp	Val	Gly	Gly	Lys	Ile	Ile	His	Lys	Ile	Ile	
				405					410					415			
30	GAT	CTG	GGA	TAT	GCC	AAA	GAT	GTT	GAT	CAA	GGA	AGT	CTG	TGT	ACA	TCT	1296
	Asp	Leu	Gly	Tyr	Ala	Lys	Asp	Val	Asp	Gln	Gly	Ser	Leu	Cys	Thr	Ser	
			420						425					430			
35	TTT	GTG	GGA	ACA	CTG	CAG	TAT	CTG	GCC	CCA	GAG	CTC	TTT	GAG	AAT	AAG	1344
	Phe	Val	Gly	Thr	Leu	Gln	Tyr	Leu	Ala	Pro	Glu	Leu	Phe	Glu	Asn	Lys	
		435					440						445				
40	CCT	TAC	ACA	GCC	ACT	GTT	GAT	TAT	TGG	AGC	TTT	GGG	ACC	ATG	GTA	TTT	1392
	Pro	Tyr	Thr	Ala	Thr	Val	Asp	Tyr	Trp	Ser	Phe	Gly	Thr	Met	Val	Phe	
		450					455					460					
45	GAA	TGT	ATT	GCT	GGA	TAT	AGG	CCT	TTT	TTG	CAT	CAT	CTG	CAG	CCA	TTT	1440
	Glu	Cys	Ile	Ala	Gly	Tyr	Arg	Pro	Phe	Leu	His	His	Leu	Gln	Pro	Phe	
	465				470				475							480	
50	ACC	TGG	CAT	GAG	AAG	ATT	AAG	AAG	AAG	GAT	CCA	AAG	TGT	ATA	TTT	GCA	1488
	Thr	Trp	His	Glu	Lys	Ile	Lys	Lys	Lys	Asp	Pro	Lys	Cys	Ile	Phe	Ala	
				485					490					495			
55	TGT	GAA	GAG	ATG	TCA	GGA	GAA	GTT	CGG	TTT	AGT	AGC	CAT	TTA	CCT	CAA	1536
	Cys	Glu	Glu	Met	Ser	Gly	Glu	Val	Arg	Phe	Ser	Ser	His	Leu	Pro	Gln	
			500						505					510			
60	CCA	AAT	AGC	CTT	TGT	AGT	TTA	ATA	GTA	GAA	CCC	ATG	GAA	AAC	TGG	CTA	1584
65	Gln	Leu	Met	Leu	Asn	Trp	Asp	Pro	Gln	Gln	Arg	Gly	Gly	Pro	Val	Asp	
		530					535					540					
70	CTT	ACT	TTG	AAG	CAG	CGA	AGC	TGT	TTT	CTA	TCT	ATG	GTT	GAA	TTT	TTG	

229

	Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met Asp His Ile Leu	
	545 550 555 560	
5	AAT TTG AAG ATA GTA CAC ATC CTA AAT ATG ACT TCT GCA AAG ATA ATT Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser Ala Lys Ile Ile	1728
	565 570 575	
10	TCT TTT CTG TTA CCA CCT GAT GAA AGT CTT CAT TCA CTA CAG TCT CGT Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser Leu Gln Ser Arg	1776
	580 585 590	
15	ATT GAG CGT GAA ACT GGA ATA AAT ACT GGT TCT CAA GAA CTT CTT TCA Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln Glu Leu Leu Ser	1824
	595 600 605	
	GAG ACA GGA ATT TCT CTG GAT CCT CGG AAA CCA GCC TCT CAA TGT GTT Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala Ser Gln Cys Val	1872
	610 615 620	
20	CTA GAT GGA GTT AGA GGC TGT GAT AGC TAT ATG GTT TAT TTG TTT GAT Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val Tyr Leu Phe Asp	1920
	625 630 635 640	
25	AAA AGT AAA ACT GTA TAT GAA GGG CCA TTT GCT TCC AGA AGT TTA TCT Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser Arg Ser Leu Ser	1968
	645 650 655	
30	GAT TGT GTA AAT TAT ATT GTA CAG GAC AGC AAA ATA CAG CTT CCA ATT Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile Gln Leu Pro Ile	2016
	660 665 670	
35	ATA CAG CTG CGT AAA GTG TGG GCT GAA GCA GTG CAC TAT GTG TCT GGA Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His Tyr Val Ser Gly	2064
	675 680 685	
	CTA AAA GAA GAC TAT AGC AGG CTC TTT CAG GGA CAA AGG GCA GCA ATG Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln Arg Ala Ala Met	2112
	690 695 700	
40	TTA AGT CTT CTT AGA TAT AAT GCT AAC TTA ACA AAA ATG AAG AAC ACT Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys Met Lys Asn Thr	2160
	705 710 715 720	
45	TTG ATC TCA GCA TCA CAA CAA CTG AAA GCT AAA TTG GAG TTT TTT CAC Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu Glu Phe Phe His	2208
	725 730 735	
	AAA AGC ATT CAG CTT GAC TTG GAG AGA TAC ACC GAG CAG ATG ACC TAT	2256
55	Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys Glu Met Glu Glu	
	755 760 765	
	AAA GGC ATC GAC TAT GGT GAG GGT GGT GGT ATT GCA TAC CTC GAG GAT	

230

	Lys	Ala	Ile	His	Tyr	Ala	Glu	Val	Gly	Val	Ile	Gly	Tyr	Leu	Glu	Asp	
	770						775					780					
5	CAG	ATT	ATG	TCT	TTG	CAT	GCT	GAA	ATC	ATG	GGG	CTA	CAG	AAG	AGC	CCC	2400
	Gln	Ile	Met	Ser	Leu	His	Ala	Glu	Ile	Met	Gly	Leu	Gln	Lys	Ser	Pro	
	785					790					795					800	
10	TAT	GGA	AGA	CGT	CAG	GGA	GAC	TTG	ATG	GAA	TCT	CTG	GAA	CAG	CGT	GCC	2448
	Tyr	Gly	Arg	Arg	Gln	Gly	Asp	Leu	Met	Glu	Ser	Leu	Glu	Gln	Arg	Ala	
					805					810					815		
15	ATT	GAT	CTA	TAT	AAG	CAG	TTA	AAA	CAC	AGA	CCT	TCA	GAT	CAC	TCC	TAC	2496
	Ile	Asp	Leu	Tyr	Lys	Gln	Leu	Lys	His	Arg	Pro	Ser	Asp	His	Ser	Tyr	
				820					825						830		
20	AGT	GAC	AGC	ACA	GAG	ATG	GTG	AAA	ATC	ATT	GTG	CAC	ACT	GTG	CAG	AGT	2544
	Ser	Asp	Ser	Thr	Glu	Met	Val	Lys	Ile	Ile	Val	His	Thr	Val	Gln	Ser	
				835				840					845				
25	CAG	GAC	CGT	GTG	CTC	AAG	GAG	CTG	TTT	GGT	CAT	TTG	AGC	AAG	TTG	TTG	2592
	Gln	Asp	Arg	Val	Leu	Lys	Glu	Leu	Phe	Gly	His	Leu	Ser	Lys	Leu	Leu	
		850					855					860					
30	GGC	TGT	AAG	CAG	AAG	ATT	ATT	GAT	CTA	CTC	CCT	AAG	GTG	GAA	GTG	GCC	2640
	Gly	Cys	Lys	Gln	Lys	Ile	Ile	Asp	Leu	Leu	Pro	Lys	Val	Glu	Val	Ala	
	865					870					875					880	
35	CTC	AGT	AAT	ATC	AAA	GAA	GCT	GAC	AAT	ACT	GTC	ATG	TTC	ATG	CAG	GGA	2688
	Leu	Ser	Asn	Ile	Lys	Glu	Ala	Asp	Asn	Thr	Val	Met	Phe	Met	Gln	Gly	
					885					890					895		
40	AAA	AGG	CAG	AAA	GAA	ATA	TGG	CAT	CTC	CTT	AAA	ATT	GCC	TGT	ACA	CAG	2736
	Lys	Arg	Gln	Lys	Glu	Ile	Trp	His	Leu	Leu	Lys	Ile	Ala	Cys	Thr	Gln	
				900					905					910			
45	AGT	TCT	GCC	CGC	TCT	CTT	GTA	GGA	TCC	AGT	CTA	GAA	GGT	GCA	GTA	ACC	2784
	Ser	Ser	Ala	Arg	Ser	Leu	Val	Gly	Ser	Ser	Leu	Glu	Gly	Ala	Val	Thr	
			915					920					925				
50	CCT	CAG	ACA	TCA	GCA	TGG	CTG	CCC	CCG	ACT	TCA	GCA	GAA	CAT	GAT	CAT	2832
	Pro	Gln	Thr	Ser	Ala	Trp	Leu	Pro	Pro	Thr	Ser	Ala	Glu	His	Asp	His	
			930				935					940					
55	TCT	CTG	TCA	TGT	GTG	GTA	ACT	CCT	CAA	GAT	GGG	GAG	ACT	TCA	GCA	CAA	2880
	Ser	Leu	Ser	Cys	Val	Val	Thr	Pro	Gln	Asp	Gly	Glu	Thr	Ser	Ala	Gln	
	945					950					955					960	
60	ATG	ATA	GAA	GAA	AAT	TTG	AAC	TGC	CTT	GGC	CAT	TTA	AGC	ACT	ATT	ATT	2928
	His	Glu	Ala	Asn	Glu	Glu	Gln	Gly	Asn	Ser	Met	Met	Asn	Leu	Asp	Trp	
				980					985					990			
65	ACT	TGG	TTA	ACA	GAA	TCA											3024

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:121:

	275		280		285
	Leu Asp	Leu Lys Ile Ala Ile	Lys Ser Cys Arg Leu	Glu Leu Ser Thr	
55	290		295		300
	Leu Asp Arg Glu Leu Tyr	Glu Val Thr Ile Thr Ile	Met Val Thr		

	305				310					315					320	
	Asn	His	Ala	Asn	Val	Val	Lys	Ala	Cys	Asp	Val	Pro	Glu	Glu	Leu	Asn
					325					330					335	
5	Ile	Leu	Ile	His	Asp	Val	Pro	Leu	Leu	Ala	Met	Glu	Tyr	Cys	Ser	Gly
				340						345					350	
	Gly	Asp	Leu	Arg	Lys	Leu	Leu	Asn	Lys	Pro	Glu	Asn	Cys	Cys	Gly	Leu
				355					360					365		
	Lys	Glu	Ser	Gln	Ile	Leu	Ser	Leu	Leu	Ser	Asp	Ile	Gly	Ser	Gly	Ile
		370					375					380				
10	Arg	Tyr	Leu	His	Glu	Asn	Lys	Ile	Ile	His	Arg	Asp	Leu	Lys	Pro	Glu
	385					390					395					400
	Asn	Ile	Val	Leu	Gln	Asp	Val	Gly	Gly	Lys	Ile	Ile	His	Lys	Ile	Ile
					405					410					415	
15	Asp	Leu	Gly	Tyr	Ala	Lys	Asp	Val	Asp	Gln	Gly	Ser	Leu	Cys	Thr	Ser
				420					425					430		
	Phe	Val	Gly	Thr	Leu	Gln	Tyr	Leu	Ala	Pro	Glu	Leu	Phe	Glu	Asn	Lys
				435					440					445		
	Pro	Tyr	Thr	Ala	Thr	Val	Asp	Tyr	Trp	Ser	Phe	Gly	Thr	Met	Val	Phe
		450					455					460				
20	Glu	Cys	Ile	Ala	Gly	Tyr	Arg	Pro	Phe	Leu	His	Leu	Gln	Pro	Phe	
	465					470					475				480	
	Thr	Trp	His	Glu	Lys	Ile	Lys	Lys	Lys	Asp	Pro	Lys	Cys	Ile	Phe	Ala
					485					490					495	
25	Cys	Glu	Glu	Met	Ser	Gly	Glu	Val	Arg	Phe	Ser	Ser	His	Leu	Pro	Gln
				500					505					510		
	Pro	Asn	Ser	Leu	Cys	Ser	Leu	Ile	Val	Glu	Pro	Met	Glu	Asn	Trp	Leu
				515					520					525		
	Gln	Leu	Met	Leu	Asn	Trp	Asp	Pro	Gln	Gln	Arg	Gly	Gly	Pro	Val	Asp
		530					535					540				
30	Leu	Thr	Leu	Lys	Gln	Pro	Arg	Cys	Phe	Val	Leu	Met	Asp	His	Ile	Leu
	545					550					555				560	
	Asn	Leu	Lys	Ile	Val	His	Ile	Leu	Asn	Met	Thr	Ser	Ala	Lys	Ile	Ile
					565					570					575	
35	Ser	Phe	Leu	Leu	Pro	Pro	Asp	Glu	Ser	Leu	His	Ser	Leu	Gln	Ser	Arg
				580					585					590		
	Ile	Glu	Arg	Glu	Thr	Gly	Ile	Asn	Thr	Gly	Ser	Gln	Glu	Leu	Leu	Ser
				595				600					605			
	Glu	Thr	Gly	Ile	Ser	Leu	Asp	Pro	Arg	Lys	Pro	Ala	Ser	Gln	Cys	Val
							615					620				
40	Leu	Asp	Gly	Val	Arg	Gly	Cys	Asp	Ser	Tyr	Met	Val	Tyr	Leu	Phe	Asp
	625					630					635				640	
	Lys	Ser	Lys	Thr	Val	Tyr	Glu	Gly	Pro	Phe	Ala	Ser	Arg	Ser	Leu	Ser
					645					650</						

233

		755				760				765				
		Lys	Ala	Ile	His	Tyr	Ala	Glu	Val	Gly	Val	Ile	Gly	Tyr
		770						775				780		
		Gln	Ile	Met	Ser	Leu	His	Ala	Glu	Ile	Met	Gly	Leu	Gln
5		785					790				795			800
		Tyr	Gly	Arg	Arg	Gln	Gly	Asp	Leu	Met	Glu	Ser	Leu	Glu
						805					810			815
		Ile	Asp	Leu	Tyr	Lys	Gln	Leu	Lys	His	Arg	Pro	Ser	Asp
					820					825				830
10		Ser	Asp	Ser	Thr	Glu	Met	Val	Lys	Ile	Ile	Val	His	Thr
									835				840	845
		Gln	Asp	Arg	Val	Leu	Lys	Glu	Leu	Phe	Gly	His	Leu	Ser
						850			855			860		
		Gly	Cys	Lys	Gln	Lys	Ile	Asp	Leu	Leu	Pro	Lys	Val	Glu
15		865					870				875			880
		Leu	Ser	Asn	Ile	Lys	Glu	Ala	Asp	Asn	Thr	Val	Met	Phe
						885					890			895
		Lys	Arg	Gln	Lys	Glu	Ile	Trp	His	Leu	Leu	Lys	Ile	Ala
						900				905				910
20		Ser	Ser	Ala	Arg	Ser	Leu	Val	Gly	Ser	Ser	Leu	Glu	Gly
									915				920	925
		Pro	Gln	Thr	Ser	Ala	Trp	Leu	Pro	Pro	Thr	Ser	Ala	Glu
						930			935				940	
		Ser	Leu	Ser	Cys	Val	Val	Thr	Pro	Gln	Asp	Gly	Glu	Thr
25		945					950				955			960
		Met	Ile	Glu	Glu	Asn	Leu	Asn	Cys	Leu	Gly	His	Leu	Ser
						965					970			975
		His	Glu	Ala	Asn	Glu	Glu	Gln	Gly	Asn	Ser	Met	Met	Asn
						980				985				990
30		Ser	Trp	Leu	Thr	Glu								
						995								

(2) INFORMATION FOR SEQ ID NO:122:

- 35 (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 2991 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- 40 (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
- (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 1...2988
 - (D) OTHER INFORMATION:
- 45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:

55	ATG	CGG	GAG	CGG	CTG	GGC	ACC	GGC	GGC	TTC	GGG	AAC	GTC	TGT	CTG	TAC
	Met	Arg	Glu	Arg	Leu	Gly	Thr	Gly	Gly	Phe	Gly	Asn	Val	Cys	Leu	Tyr
					20					25						

96

234

	CAG CAT CGG GAA CTT GAT CTC AAA ATA GCA ATT AAG TCT TGT CGC CTA	144
	Gln His Arg Glu Leu Asp Leu Lys Ile Ala Ile Lys Ser Cys Arg Leu	
	35 40 45	
5	GAG CTA AGT ACC AAA AAC AGA GAA CGA TGG TGC CAT GAA ATC CAG ATT	192
	Glu Leu Ser Thr Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile	
	50 55 60	
10	ATG AAG AAG TTG AAC CAT GCC AAT GTT GTA AAG GCC TGT GAT GTT CCT	240
	Met Lys Lys Leu Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro	
	65 70 75 80	
15	GAA GAA TTG AAT ATT TTG ATT CAT GAT GTG CCT CTT CTA GCA ATG GAA	288
	Glu Glu Leu Asn Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu	
	85 90 95	
20	TAC TGT TCT GGA GGA GAT CTC CGA AAG CTG CTC AAC AAA CCA GAA AAT	336
	Tyr Cys Ser Gly Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn	
	100 105 110	
25	TGT TGT GGA CTT AAA GAA AGC CAG ATA CTT TCT TTA CTA AGT GAT ATA	384
	Cys Cys Gly Leu Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile	
	115 120 125	
30	GGG TCT GGG ATT CGA TAT TTG CAT GAA AAC AAA ATT ATA CAT CGA GAT	432
	Gly Ser Gly Ile Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp	
	130 135 140	
35	CTA AAA CCT GAA AAC ATA GTT CTT CAG GAT GTT GGT GGA AAG ATA ATA	480
	Leu Lys Pro Glu Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile	
	145 150 155 160	
40	CAT AAA ATA ATT GAT CTG GGA TAT GCC AAA GAT GTT GAT CAA GGA AGT	528
	His Lys Ile Ile Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser	
	165 170 175	
45	CTG TGT ACA TCT TTT GTG GGA ACA CTG CAG TAT CTG GCC CCA GAG CTC	576
	Leu Cys Thr Ser Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu	
	180 185 190	
50	TTT GAG AAT AAG CCT TAC ACA GCC ACT GTT GAT TAT TGG AGC TTT GGG	624
	Phe Glu Asn Lys Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly	
	195 200 205	
55	ACC ATG GTA TTT GAA TGT ATT GCT GGA TAT AGG CCT TTT TTG CAT CAT	672
	Thr Met Val Phe Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His	
	210 215 220	
60	TGT ATA TTT GCA TGT GAA GAG ATG TCA GGA GAA GTT CGG TTT AGT AGC	768
	Cys Ile Phe Ala Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser	
	225 230 235	

235

	CAT	TTA	CCT	CAA	CCA	AAT	AGC	CTT	TGT	AGT	TTA	ATA	GTA	GAA	CCC	ATG	816
	His	Leu	Pro	Gln	Pro	Asn	Ser	Leu	Cys	Ser	Leu	Ile	Val	Glu	Pro	Met	
				260					265					270			
5	GAA	AAC	TGG	CTA	CAG	TTG	ATG	TTG	AAT	TGG	GAC	CCT	CAG	CAG	AGA	GGA	864
	Glu	Asn	Trp	Leu	Gln	Leu	Met	Leu	Asn	Trp	Asp	Pro	Gln	Gln	Arg	Gly	
			275					280					285				
10	GGA	CCT	GTT	GAC	CTT	ACT	TTG	AAG	CAG	CCA	AGA	TGT	TTT	GTA	TTA	ATG	912
	Gly	Pro	Val	Asp	Leu	Thr	Leu	Lys	Gln	Pro	Arg	Cys	Phe	Val	Leu	Met	
			290					295					300				
15	GAT	CAC	ATT	TTG	AAT	TTG	AAG	ATA	GTA	CAC	ATC	CTA	AAT	ATG	ACT	TCT	960
	Asp	His	Ile	Leu	Asn	Leu	Lys	Ile	Val	His	Ile	Leu	Asn	Met	Thr	Ser	
	305					310					315					320	
20	GCA	AAG	ATA	ATT	TCT	TTT	CTG	TTA	CCA	CCT	GAT	GAA	AGT	CTT	CAT	TCA	1008
	Ala	Lys	Ile	Ile	Ser	Phe	Leu	Leu	Pro	Pro	Asp	Glu	Ser	Leu	His	Ser	
					325					330					335		
25	CTA	CAG	TCT	CGT	ATT	GAG	CGT	GAA	ACT	GGA	ATA	AAT	ACT	GGT	TCT	CAA	1056
	Leu	Gln	Ser	Arg	Ile	Glu	Arg	Glu	Thr	Gly	Ile	Asn	Thr	Gly	Ser	Gln	
				340					345					350			
30	GAA	CTT	CTT	TCA	GAG	ACA	GGA	ATT	TCT	CTG	GAT	CCT	CGG	AAA	CCA	GCC	1104
	Glu	Leu	Leu	Ser	Glu	Thr	Gly	Ile	Ser	Leu	Asp	Pro	Arg	Lys	Pro	Ala	
			355					360					365				
35	TAT	TTG	TTT	GAT	AAA	AGT	AAA	ACT	GTA	TAT	GAA	GGG	CCA	TTT	GCT	TCC	1200
	Tyr	Leu	Phe	Asp	Lys	Ser	Lys	Thr	Val	Tyr	Glu	Gly	Pro	Phe	Ala	Ser	
	385					390					395					400	
40	AGA	AGT	TTA	TCT	GAT	TGT	GTA	AAT	TAT	ATT	GTA	CAG	GAC	AGC	AAA	ATA	1248
	Arg	Ser	Leu	Ser	Asp	Cys	Val	Asn	Tyr	Ile	Val	Gln	Asp	Ser	Lys	Ile	
					405					410					415		
45	CAG	CTT	CCA	ATT	ATA	CAG	CTG	CGT	AAA	GTG	TGG	GCT	GAA	GCA	GTG	CAC	1296
	Gln	Leu	Pro	Ile	Ile	Gln	Leu	Arg	Lys	Val	Trp	Ala	Glu	Ala	Val	His	
				420					425					430			
50	TAT	GTG	TCT	GGA	CTA	AAA	GAA	GAC	TAT	AGC	AGG	CTC	TTT	CAG	GGA	CAA	1344
	Tyr	Val	Ser	Gly	Leu	Lys	Glu	Asp	Tyr	Ser	Arg	Leu	Phe	Gln	Gly	Gln	
			435					440					445				
55	ATG	AAG	AAC	ACT	TTG	ATC	TCA	GCA	TCA	CAA	CAA	CTG	AAA	GCT	AAA	TTG	1440
	Met	Lys	Asn	Thr	Leu	Ile	Ser	Ala	Ser	Gln	Gln	Leu	Lys	Ala	Lys	Leu	
	465					470					475					480	

236

	GAG TTT TTT CAC AAA AGC ATT CAG CTT GAC TTG GAG AGA TAC AGC GAG	1488
	Glu Phe Phe His Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu	
	485 490 495	
5	CAG ATG ACG TAT GGG ATA TCT TCA GAA AAA ATG CTA AAA GCA TGG AAA	1536
	Gln Met Thr Tyr Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys	
	500 505 510	
10	GAA ATG GAA GAA AAG GCC ATC CAC TAT GCT GAG GTT GGT GTC ATT GGA	1584
	Glu Met Glu Glu Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly	
	515 520 525	
15	TAC CTG GAG GAT CAG ATT ATG TCT TTG CAT GCT GAA ATC ATG GGG CTA	1632
	Tyr Leu Glu Asp Gln Ile Met Ser Leu His Ala Glu Ile Met Gly Leu	
	530 535 540	
20	CAG AAG AGC CCC TAT GGA AGA CGT CAG GGA GAC TTG ATG GAA TCT CTG	1680
	Gln Lys Ser Pro Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu	
	545 550 555 560	
25	GAA CAG CGT GCC ATT GAT CTA TAT AAG CAG TTA AAA CAC AGA CCT TCA	1728
	Glu Gln Arg Ala Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser	
	565 570 575	
	GAT CAC TCC TAC AGT GAC AGC ACA GAG ATG GTG AAA ATC ATT GTG CAC	1776
	Asp His Ser Tyr Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His	
	580 585 590	
30	ACT GTG CAG AGT CAG GAC CGT GTG CTC AAG GAG CTG TTT GGT CAT TTG	1824
	Thr Val Gln Ser Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu	
	595 600 605	
35	AGC AAG TTG TTG GGC TGT AAG CAG AAG ATT ATT GAT CTA CTC CCT AAG	1872
	Ser Lys Leu Leu Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys	
	610 615 620	
40	GTG GAA GTG GCC CTC AGT AAT ATC AAA GAA GCT GAC AAT ACT GTC ATG	1920
	Val Glu Val Ala Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met	
	625 630 635 640	
45	TTC ATG CAG GGA AAA AGG CAG AAA GAA ATA TGG CAT CTC CTT AAA ATT	1968
	Phe Met Gln Gly Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile	
	645 650 655	
	GCC TGT ACA CAG AGT TCT GCC CGC TCT CTT GTA GGA TCC AGT CTA GAA	2016
	Ala Cys Thr Gln Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu	
	660 665 670	
55	GAA CAT GAT CAT TCT CTG TCA TGT GTG GTA ACT CCT CAA GAT GGG GAG	2112
	Glu His Asp His Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu	
	675 680 685	

237

5	ACT TCA GCA CAA ATG ATA GAA GAA AAT TTG AAC TGC CTT GGC CAT TTA	2160
	Thr Ser Ala Gln Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu	
	705 710 715 720	
10	AGC ACT ATT ATT CAT GAG GCA AAT GAG GAA CAG GGC AAT AGT ATG ATG	2208
	Ser Thr Ile Ile His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met	
	725 730 735	
15	AAT CTT GAT TGG AGT TGG TTA ACA GAA TGG GTA CCG CGG GCC CGG GAT	2256
	Asn Leu Asp Trp Ser Trp Leu Thr Glu Trp Val Pro Arg Ala Arg Asp	
	740 745 750	
20	CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG	2304
	Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly	
	755 760 765	
25	GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG	2352
	Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys	
	770 775 780	
30	TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG	2400
	Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu	
	785 790 795 800	
35	ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC	2448
	Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro	
	805 810 815	
40	ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC	2496
	Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr	
	820 825 830	
45	CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA	2544
	Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu	
	835 840 845	
50	GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC	2592
	Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr	
	850 855 860	
55	AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC	2640
	Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg	
	865 870 875 880	
60	ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG	2688
	Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly	
	885 890 895	
65	GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC	2784
	Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn	
	915 920 925	

238

5 ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC 2832
 Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
 930 935 940
 CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC 2880
 Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
 945 950 955 960
 10 ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG 2928
 Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
 965 970 975
 15 GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC 2976
 Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
 980 985 990
 GAG CTG TAC AAG TAA 2991
 Glu Leu Tyr Lys
 20 995

(2) INFORMATION FOR SEQ ID NO:123:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 996 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: protein
 (v) FRAGMENT TYPE: internal

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:

35 Met Glu Arg Pro Pro Gly Leu Arg Pro Gly Ala Gly Gly Pro Trp Glu
 1 5 10 15
 Met Arg Glu Arg Leu Gly Thr Gly Gly Phe Gly Asn Val Cys Leu Tyr
 20 25 30
 40 Gln His Arg Glu Leu Asp Leu Lys Ile Ala Ile Lys Ser Cys Arg Leu
 35 40 45
 Glu Leu Ser Thr Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile
 50 55 60
 45 Met Lys Lys Leu Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro
 65 70 75 80
 Glu Glu Leu Asn Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu
 85 90 95
 Tyr Cys Ser Gly Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asp
 130 135 140
 55 Leu Lys Pro Glu Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile
 145 150 155 160
 His Lys Ile Ile Asp Leu Gly Tyr Ala Lys Asp Val Asn Glu Gly Glu

					165					170					175	
	Leu	Cys	Thr	Ser	Phe	Val	Gly	Thr	Leu	Gln	Tyr	Leu	Ala	Pro	Glu	Leu
				180					185					190		
5	Phe	Glu	Asn	Lys	Pro	Tyr	Thr	Ala	Thr	Val	Asp	Tyr	Trp	Ser	Phe	Gly
			195					200					205			
	Thr	Met	Val	Phe	Glu	Cys	Ile	Ala	Gly	Tyr	Arg	Pro	Phe	Leu	His	His
			210				215					220				
	Leu	Gln	Pro	Phe	Thr	Trp	His	Glu	Lys	Ile	Lys	Lys	Lys	Asp	Pro	Lys
	225					230					235					240
10	Cys	Ile	Phe	Ala	Cys	Glu	Glu	Met	Ser	Gly	Glu	Val	Arg	Phe	Ser	Ser
					245					250					255	
	His	Leu	Pro	Gln	Pro	Asn	Ser	Leu	Cys	Ser	Leu	Ile	Val	Glu	Pro	Met
				260				265						270		
15	Glu	Asn	Trp	Leu	Gln	Leu	Met	Leu	Asn	Trp	Asp	Pro	Gln	Gln	Arg	Gly
			275					280					285			
	Gly	Pro	Val	Asp	Leu	Thr	Leu	Lys	Gln	Pro	Arg	Cys	Phe	Val	Leu	Met
		290				295						300				
	Asp	His	Ile	Leu	Asn	Leu	Lys	Ile	Val	His	Ile	Leu	Asn	Met	Thr	Ser
	305					310					315					320
20	Ala	Lys	Ile	Ile	Ser	Phe	Leu	Leu	Pro	Pro	Asp	Glu	Ser	Leu	His	Ser
					325					330					335	
	Leu	Gln	Ser	Arg	Ile	Glu	Arg	Glu	Thr	Gly	Ile	Asn	Thr	Gly	Ser	Gln
				340				345						350		
25	Glu	Leu	Leu	Ser	Glu	Thr	Gly	Ile	Ser	Leu	Asp	Pro	Arg	Lys	Pro	Ala
			355				360						365			
	Ser	Gln	Cys	Val	Leu	Asp	Gly	Val	Arg	Gly	Cys	Asp	Ser	Tyr	Met	Val
		370				375					380					
	Tyr	Leu	Phe	Asp	Lys	Ser	Lys	Thr	Val	Tyr	Glu	Gly	Pro	Phe	Ala	Ser
	385					390					395					400
30	Arg	Ser	Leu	Ser	Asp	Cys	Val	Asn	Tyr	Ile	Val	Gln	Asp	Ser	Lys	Ile
					405					410					415	
	Gln	Leu	Pro	Ile	Ile	Gln	Leu	Arg	Lys	Val	Trp	Ala	Glu	Ala	Val	His
				420				425						430		
35	Tyr	Val	Ser	Gly	Leu	Lys	Glu	Asp	Tyr	Ser	Arg	Leu	Phe	Gln	Gly	Gln
			435				440						445			
	Arg	Ala	Ala	Met	Leu	Ser	Leu	Leu	Arg	Tyr	Asn	Ala	Asn	Leu	Thr	Lys
		450					455					460				
	Met	Lys	Asn	Thr	Leu	Ile	Ser	Ala	Ser	Gln	Gln	Leu	Lys	Ala	Lys	Leu
	465					470					475					480
40	Glu	Phe	Phe	His	Lys	Ser	Ile	Gln	Leu	Asp	Leu	Glu	Arg	Tyr	Ser	Glu
				485						490					495	
	Gln	Met	Thr	Tyr	Gly	Ile	Ser	Ser	Glu	Lys	Met	Leu	L			

240

	610		615		620	
	Val Glu Val Ala Leu	Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met				
	625	630	635	640		
	Phe Met Gln Gly Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile					
5		645	650	655		
	Ala Cys Thr Gln Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu					
	660	665	670			
	Gly Ala Val Thr Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala					
	675	680	685			
10	Glu His Asp His Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu					
	690	695	700			
	Thr Ser Ala Gln Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu					
	705	710	715	720		
	Ser Thr Ile Ile His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met					
15		725	730	735		
	Asn Leu Asp Trp Ser Trp Leu Thr Glu Trp Val Pro Arg Ala Arg Asp					
	740	745	750			
	Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly					
	755	760	765			
20	Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys					
	770	775	780			
	Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu					
	785	790	795	800		
	Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro					
25		805	810	815		
	Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr					
	820	825	830			
	Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu					
	835	840	845			
30	Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr					
	850	855	860			
	Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg					
	865	870	875	880		
	Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly					
35		885	890	895		
	His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala					
	900	905	910			
	Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn					
	915	920	925			
40	Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr					
	930	935	940			
	Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser					
	945	950	955	960		
	Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met					
45		965	970	975		
	Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp					
	980	985	990			
	Glu Leu Tyr Lys					

1. SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1908 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

55

241

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

5

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...1905

(D) OTHER INFORMATION:

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:124:

15	ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu 1 5 10 15	48
15	GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly 20 25 30	96
20	GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile 35 40 45	144
25	TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr 50 55 60	192
30	CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys 65 70 75 80	240
35	CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu 85 90 95	288
35	CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu 100 105 110	336
40	GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly 115 120 125	384
45	ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr 130 135 140	432
55	AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC Asn Thr Asn Ser Gln Gln Thr Ile Arg His Asn Ile Glu Asp Gly Ser 165 170 175	480
55	GTG CAG CTG GCC GAG CAG TAC CAG CAG AAC ACC GGC ATC GGC GAG GGC	528

242

	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	
				180					185					190			
5	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	ACC	CAG	TCC	GCC	CTG	624
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	
			195				200						205				
10	AGC	AAA	GAC	CCC	AAC	GAG	AAG	CGC	GAT	CAC	ATG	GTC	CTG	CTG	GAG	TTC	672
	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	
		210					215					220					
15	GTG	ACC	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	GAG	CTG	TAC	AAG	TCC	720
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser	
	225					230					235					240	
	GGA	CTC	AGA	TCT	CGA	GCT	CAA	GCT	TCC	ATG	AGC	GAG	ACG	GTC	ATC	ATG	768
	Gly	Leu	Arg	Ser	Arg	Ala	Gln	Ala	Ser	Met	Ser	Glu	Thr	Val	Ile	Met	
					245					250					255		
20	AGC	GAG	ACG	GTC	ATC	TGT	TCC	AGC	CGG	GCC	ACT	GTG	ATG	CTT	TAT	GAT	816
	Ser	Glu	Thr	Val	Ile	Cys	Ser	Ser	Arg	Ala	Thr	Val	Met	Leu	Tyr	Asp	
				260					265					270			
25	GAT	GGC	AAC	AAG	CGA	TGG	CTC	CCT	GCT	GGC	ACG	GGT	CCC	CAG	GCC	TTC	864
	Asp	Gly	Asn	Lys	Arg	Trp	Leu	Pro	Ala	Gly	Thr	Gly	Pro	Gln	Ala	Phe	
			275					280					285				
30	AGC	CGC	GTC	CAG	ATC	TAC	CAC	AAC	CCC	ACG	GCC	AAT	TCC	TTT	CGC	GTC	912
	Ser	Arg	Val	Gln	Ile	Tyr	His	Asn	Pro	Thr	Ala	Asn	Ser	Phe	Arg	Val	
		290					295					300					
35	GTG	GGC	CGG	AAG	ATG	CAG	CCC	GAC	CAG	CAG	GTG	GTC	ATC	AAC	TGT	GCC	960
	Val	Gly	Arg	Lys	Met	Gln	Pro	Asp	Gln	Gln	Val	Val	Ile	Asn	Cys	Ala	
	305					310					315					320	
	ATC	GTC	CGG	GGT	GTG	AAG	TAT	AAC	CAG	GCC	ACC	CCC	AAC	TTC	CAT	CAG	1008
	Ile	Val	Arg	Gly	Val	Lys	Tyr	Asn	Gln	Ala	Thr	Pro	Asn	Phe	His	Gln	
					325					330				335			
40	TGG	CGC	GAC	GCT	CGC	CAG	GTC	TGG	GGC	CTC	AAC	TTC	GGC	AGC	AAG	GAG	1056
	Trp	Arg	Asp	Ala	Arg	Gln	Val	Trp	Gly	Leu	Asn	Phe	Gly	Ser	Lys	Glu	
				340					345					350			
45	GAT	GCG	GCC	CAG	TTT	GCC	GCC	GGC	ATG	GCC	AGT	GCC	CTA	GAG	GCG	TTG	1104
	Asp	Ala	Ala	Gln	Phe	Ala	Ala	Gly	Met	Ala	Ser	Ala	Leu	Glu	Ala	Leu	
			355					360					365				
	GAA	GGA	GGT	GGG	CCC	CCT	CCA	CCC	CCA	GCA	CTT	CCC	ACC	TGG	TCG	GTC	1152
55	CCC	GGC	CCG	TCG	GAG	CAC	ATA	GAG	CGC	GGG	GTC	TCC	AAT	GCA	GCA	GCC	1216

	Pro	Gly	Pro	Ser	Glu	His	Ile	Glu	Arg	Arg	Val	Ser	Asn	Ala	Gly	Gly	
					405					410					415		
5	CCA	CCT	GCT	CCC	CCC	GCT	GGG	GGT	CCA	CCC	CCA	CCA	CCA	GGA	CCT	CCC	1296
	Pro	Pro	Ala	Pro	Pro	Ala	Gly	Gly	Pro	Pro	Pro	Pro	Pro	Gly	Pro	Pro	
				420					425					430			
10	CCT	CCT	CCA	GGT	CCC	CCC	CCA	CCC	CCA	GGT	TTG	CCC	CCT	TCG	GGG	GTC	1344
	Pro	Pro	Pro	Gly	Pro	Pro	Pro	Pro	Pro	Gly	Leu	Pro	Pro	Ser	Gly	Val	
				435				440					445				
15	CCA	GCT	GCA	GCG	CAC	GGA	GCA	GGG	GGA	GGA	CCA	CCC	CCT	GCA	CCC	CCT	1392
	Pro	Ala	Ala	Ala	His	Gly	Ala	Gly	Gly	Gly	Pro	Pro	Pro	Ala	Pro	Pro	
		450					455					460					
20	CTC	CCG	GCA	GCA	CAG	GGC	CCT	GGT	GGT	GGG	GGA	GCT	GGG	GCC	CCA	GGC	1440
	Leu	Pro	Ala	Ala	Gln	Gly	Pro	Gly	Gly	Gly	Gly	Ala	Gly	Ala	Pro	Gly	
	465				470					475					480		
25	CTG	GCC	GCA	GCT	ATT	GCT	GGA	GCC	AAA	CTC	AGG	AAA	GTC	AGC	AAG	CAG	1488
	Leu	Ala	Ala	Ala	Ile	Ala	Gly	Ala	Lys	Leu	Arg	Lys	Val	Ser	Lys	Gln	
					485				490						495		
30	GAG	GAG	GCC	TCA	GGG	GGG	CCC	ACA	GCC	CCC	AAA	GCT	GAG	AGT	GGT	CGA	1536
	Glu	Glu	Ala	Ser	Gly	Gly	Pro	Thr	Ala	Pro	Lys	Ala	Glu	Ser	Gly	Arg	
				500				505					510				
35	AGC	GGA	GGT	GGG	GGA	CTC	ATG	GAA	GAG	ATG	AAC	GCC	ATG	CTG	GCC	CGG	1584
	Ser	Gly	Gly	Gly	Gly	Leu	Met	Glu	Glu	Met	Asn	Ala	Met	Leu	Ala	Arg	
			515					520					525				
40	AGA	AGG	AAA	GCC	ACG	CAA	GTT	GGG	GAG	AAA	ACC	CCC	AAG	GAT	GAA	TCT	1632
	Arg	Arg	Lys	Ala	Thr	Gln	Val	Gly	Glu	Lys	Thr	Pro	Lys	Asp	Glu	Ser	
		530					535					540					
45	GCC	AAT	CAG	GAG	GAG	CCA	GAG	GCC	AGA	GTC	CCG	GCC	CAG	AGT	GAA	TCT	1680
	Ala	Asn	Gln	Glu	Glu	Pro	Glu	Ala	Arg	Val	Pro	Ala	Gln	Ser	Glu	Ser	
	545					550				555					560		
50	GTG	CGG	AGA	CCC	TGG	GAG	AAG	AAC	AGC	ACA	ACC	TTG	CCA	AGG	ATG	AAG	1728
	Val	Arg	Arg	Pro	Trp	Glu	Lys	Asn	Ser	Thr	Thr	Leu	Pro	Arg	Met	Lys	
					565				570						575		
55	TCG	TCT	TCT	TCG	GTG	ACC	ACT	TCC	GAG	ACC	CAA	CCC	TGC	ACG	CCC	AGC	1776
	Ser	Ser	Ser	Ser	Val	Thr	Thr	Ser	Glu	Thr	Gln	Pro	Cys	Thr	Pro	Ser	
				580				585					590				
	TCG	ACT	GAT	TAC	TGG	GAG	GTA	GAG	AGG	GTC	AAA	GAG	GAG	GTC	GTC	GAA	1824
	Ser	Thr	Asp	Tyr	Trp	Glu	Val	Glu	Lys	Val	Lys	Glu	Glu	Ile	Ile	Glu	
				600				605			</						

244

Phe Val Gln Glu Leu Arg Lys Arg Gly Ser Pro
 625 630 635

5 (2) INFORMATION FOR SEQ ID NO:125:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 635 amino acids

(B) TYPE: amino acid

10 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:125:

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1 5 10 15
 20 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
 20 25 30
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
 35 40 45
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 25 50 55 60
 Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
 65 70 75 80
 Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
 85 90 95
 30 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
 100 105 110
 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
 115 120 125
 Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
 35 130 135 140
 Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
 145 150 155 160
 Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
 165 170 175
 40 Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
 180 185 190
 Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
 195 200 205
 Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
 45 210 215 220
 Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
 225 230 235 240
 Gly Leu Arg Ser Arg Ala Gln Ala Ser Met Ser Glu Thr Val Ile Met
 275 280 285
 Ser Arg Val Gln Ile Tyr His Asn Pro Thr Ala Asn Ser Phe Arg Val
 55 290 295 300
 Val Glu Arg Lys Met Gln Pro Arg Val Thr Val Ile Thr Arg Val

245

	305				310				315				320
	Ile	Val	Arg	Gly	Val	Lys	Tyr	Asn	Gln	Ala	Thr	Pro	Asn
					325					330			335
	Trp	Arg	Asp	Ala	Arg	Gln	Val	Trp	Gly	Leu	Asn	Phe	Gly
5				340					345				350
	Asp	Ala	Ala	Gln	Phe	Ala	Ala	Gly	Met	Ala	Ser	Ala	Leu
				355					360				365
	Glu	Gly	Gly	Gly	Pro	Pro	Pro	Pro	Pro	Ala	Leu	Pro	Thr
				370					375				380
10	Pro	Asn	Gly	Pro	Ser	Pro	Glu	Glu	Val	Glu	Gln	Gln	Lys
	385												400
	Pro	Gly	Pro	Ser	Glu	His	Ile	Glu	Arg	Arg	Val	Ser	Asn
				405						410			415
	Pro	Pro	Ala	Pro	Pro	Ala	Gly	Gly	Pro	Pro	Pro	Pro	Gly
15				420						425			430
	Pro	Pro	Pro	Gly	Pro	Pro	Pro	Pro	Pro	Gly	Leu	Pro	Pro
				435						440			445
	Pro	Ala	Ala	Ala	His	Gly	Ala	Gly	Gly	Gly	Pro	Pro	Pro
				450									460
20	Leu	Pro	Ala	Ala	Gln	Gly	Pro	Gly	Gly	Gly	Gly	Ala	Gly
	465									475			480
	Leu	Ala	Ala	Ala	Ile	Ala	Gly	Ala	Lys	Leu	Arg	Lys	Val
				485						490			495
25	Glu	Glu	Ala	Ser	Gly	Gly	Pro	Thr	Ala	Pro	Lys	Ala	Glu
				500						505			510
	Ser	Gly	Gly	Gly	Gly	Leu	Met	Glu	Glu	Met	Asn	Ala	Met
				515						520			525
	Arg	Arg	Lys	Ala	Thr	Gln	Val	Gly	Glu	Lys	Thr	Pro	Lys
				530						535			540
30	Ala	Asn	Gln	Glu	Glu	Pro	Glu	Ala	Arg	Val	Pro	Ala	Gln
	545												560
	Val	Arg	Arg	Pro	Trp	Glu	Lys	Asn	Ser	Thr	Thr	Leu	Pro
				565						570			575
	Ser	Ser	Ser	Ser	Val	Thr	Thr	Ser	Glu	Thr	Gln	Pro	Cys
35													
				580						585			590
	Ser	Ser	Asp	Tyr	Ser	Asp	Leu	Gln	Arg	Val	Lys	Gln	Glu
				595						600			605
	Glu	Val	Lys	Lys	Glu	Leu	Gln	Lys	Val	Lys	Glu	Glu	Ile
				610						615			620
40	Phe	Val	Gln	Glu	Leu	Arg	Lys	Arg	Gly	Ser	Pro		
	625									630			635

(2) INFORMATION FOR SEQ ID NO:126:

- 45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1329 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single

FEATURE

- 55 (A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...1326
 (C) OTHER INFORMATION:

246

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:126:

5	ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu 1 5 10 15	48
10	GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly 20 25 30	96
15	GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile 35 40 45	144
20	TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr 50 55 60	192
25	CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys 65 70 75 80	240
30	CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu 85 90 95	288
35	CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu 100 105 110	336
40	GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly 115 120 125	384
45	ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr 130 135 140	432
50	AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn 145 150 155 160	480
55	GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser 165 170 175	528
60	Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu 195 200 205	

247

	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	
	210						215					220					
5	GTG	ACC	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	GAG	CTG	TAC	AAG	TCC	720
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser	
	225					230				235						240	
10	GGA	CTC	AGA	TCT	CGA	GCT	CAA	GCT	TCA	ATG	GCT	GCC	ATC	CGG	AAG	AAA	768
	Gly	Leu	Arg	Ser	Arg	Ala	Gln	Ala	Ser	Met	Ala	Ala	Ile	Arg	Lys	Lys	
					245					250					255		
15	CTG	GTG	ATT	GTT	GGT	GAT	GGA	GCC	TGT	GGA	AAG	ACA	TGC	TTG	CTC	ATA	816
	Leu	Val	Ile	Val	Gly	Asp	Gly	Ala	Cys	Gly	Lys	Thr	Cys	Leu	Leu	Ile	
				260					265					270			
20	GTC	TTC	AGC	AAG	GAC	CAG	TTC	CCA	GAG	GTG	TAT	GTG	CCC	ACA	GTG	TTT	864
	Val	Phe	Ser	Lys	Asp	Gln	Phe	Pro	Glu	Val	Tyr	Val	Pro	Thr	Val	Phe	
			275					280					285				
25	GAG	AAC	TAT	GTG	GCA	GAT	ATC	GAG	GTG	GAT	GGA	AAG	CAG	GTA	GAG	TTG	912
	Glu	Asn	Tyr	Val	Ala	Asp	Ile	Glu	Val	Asp	Gly	Lys	Gln	Val	Glu	Leu	
		290					295					300					
30	GCT	TTG	TGG	GAC	ACA	GCT	GGG	CAG	GAA	GAT	TAT	GAT	CGC	CTG	AGG	CCC	960
	Ala	Leu	Trp	Asp	Thr	Ala	Gly	Gln	Glu	Asp	Tyr	Asp	Arg	Leu	Arg	Pro	
	305					310					315					320	
35	CTC	TCC	TAC	CCA	GAT	ACC	GAT	GTT	ATA	CTG	ATG	TGT	TTT	TCC	ATC	GAC	1008
	Leu	Ser	Tyr	Pro	Asp	Thr	Asp	Val	Ile	Leu	Met	Cys	Phe	Ser	Ile	Asp	
					325					330					335		
40	AGC	CCT	GAT	AGT	TTA	GAA	AAC	ATC	CCA	GAA	AAG	TGG	ACC	CCA	GAA	GTC	1056
	Ser	Pro	Asp	Ser	Leu	Glu	Asn	Ile	Pro	Glu	Lys	Trp	Thr	Pro	Glu	Val	
				340					345					350			
45	AAG	CAT	TTC	TGT	CCC	AAC	GTG	CCC	ATC	ATC	CTG	GTT	GGG	AAT	AAG	AAG	1104
	Lys	His	Phe	Cys	Pro	Asn	Val	Pro	Ile	Ile	Leu	Val	Gly	Asn	Lys	Lys	
			355					360					365				
50	GAT	CTT	CGG	AAT	GAT	GAG	CAC	ACA	AGG	CGG	GAG	CTA	GCC	AAG	ATG	AAG	1152
	Asp	Leu	Arg	Asn	Asp	Glu	His	Thr	Arg	Arg	Glu	Leu	Ala	Lys	Met	Lys	
		370					375					380					
55	CAG	GAG	CCG	GTG	AAA	CCT	GAA	GAA	GGC	AGA	GAT	ATG	GCA	AAC	AGG	ATT	1200
	Gln	Glu	Pro	Val	Lys	Pro	Glu	Glu	Gly	Arg	Asp	Met	Ala	Asn	Arg	Ile	
	385					390					395					400	
60	GGC	GCT	TTT	GGG	TAC	ATG	GAG	TGT	TCA	GCA	AAG	ACC	AAA	GAT	GGA	GTG	1248
	Arg	Glu	Val	Phe	Glu	Met	Ala	Thr	Arg	Ala	Ala	Leu	Gln	Ala	Arg	Arg	
				420					425				430				
65	GGG	AAG	AAA	AAA	TCT	GCT	TCC	GCT	GTC	TTG	TGA						

248

Gly Lys Lys Lys Ser Gly Cys Leu Val Leu
435 440

5 (2) INFORMATION FOR SEO ID NO:127:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 442 amino acids

(B) TYPE: amino acid

```

10          (C) STRANDEDNESS: single

```

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:127:

	Met	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu
	1				5					10					15	
20	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly
				20					25					30		
	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile
				35				40						45		
25	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr
	50						55					60				
	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys
	65					70					75					80
	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu
					85					90					95	
30	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu
				100					105					110		
	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly
				115				120					125			
35	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr
	130						135					140				
	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn
	145					150					155					160
	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser
					165					170					175	
40	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly
				180					185					190		
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu
				195			200						205			
45	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe
	210						215					220				
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser
	225					230					235					240
	Gly	Leu	Arg	Ser	Arg	Ala	Gln	Ala	Ser	Met	Ala	Ala	Ile	Arg	Lys	Lys

55

		275						280						285				
	Glu	Asn	Tyr	Val	Ala	Asp	Ile	Glu	Val	Asp	Gly	Lys	Gln	Val	Glu	Leu		
		290					295					300						

249

305 310 315 320
 Leu Ser Tyr Pro Asp Thr Asp Val Ile Leu Met Cys Phe Ser Ile Asp
 325 330 335
 Ser Pro Asp Ser Leu Glu Asn Ile Pro Glu Lys Trp Thr Pro Glu Val
 5 340 345 350
 Lys His Phe Cys Pro Asn Val Pro Ile Ile Leu Val Gly Asn Lys Lys
 355 360 365
 Asp Leu Arg Asn Asp Glu His Thr Arg Arg Glu Leu Ala Lys Met Lys
 370 375 380
 10 Gln Glu Pro Val Lys Pro Glu Glu Gly Arg Asp Met Ala Asn Arg Ile
 385 390 395 400
 Gly Ala Phe Gly Tyr Met Glu Cys Ser Ala Lys Thr Lys Asp Gly Val
 405 410 415
 Arg Glu Val Phe Glu Met Ala Thr Arg Ala Ala Leu Gln Ala Arg Arg
 15 420 425 430
 Gly Lys Lys Lys Ser Gly Cys Leu Val Leu
 435 440

(2) INFORMATION FOR SEQ ID NO:128:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1140 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

25

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

30

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...1137

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:128:

35

ATG GAC CAT TAT GAT TCT CAG CAA ACC AAC GAT TAC ATG CAG CCA GAA 48
 Met Asp His Tyr Asp Ser Gln Gln Thr Asn Asp Tyr Met Gln Pro Glu
 1 5 10 15

40

GAG GAC TGG GAC CGG GAC CTG CTC CTG GAC CCG GCC TGG GAG AAG CAG 96
 Glu Asp Trp Asp Arg Asp Leu Leu Leu Asp Pro Ala Trp Glu Lys Gln
 20 25 30

45

CAG AGA AAG ACA TTC ACG GCA TGG TGT AAC TCC CAC CTC CGG AAG GCG 144
 Gln Arg Lys Thr Phe Thr Ala Trp Cys Asn Ser His Leu Arg Lys Ala
 35 40 45

GGG ACA CAG ATC GAG AAC ATC GAA GAG GAG TTC CGG GAT GCG CTC AAC 180

55

Leu Met Leu Leu Leu Glu Val Ile Ser Gly Glu Arg Leu Ala Lys Pro
 65 70 75 80

GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG GAG

250																	
	Glu	Arg	Gly	Lys	Met	Arg	Val	His	Lys	Ile	Ser	Asn	Val	Asn	Lys	Ala	
				85						90					95		
5	CTG	GAT	TTC	ATA	GCC	AGC	AAA	GGC	GTC	AAA	CTG	GTG	TCC	ATC	GGA	GCC	336
	Leu	Asp	Phe	Ile	Ala	Ser	Lys	Gly	Val	Lys	Leu	Val	Ser	Ile	Gly	Ala	
				100					105					110			
10	GAA	GAA	ATC	GTG	GAT	GGG	AAT	GTG	AAG	ATG	ACC	CTG	GGC	ATG	ATC	TGG	384
	Glu	Glu	Ile	Val	Asp	Gly	Asn	Val	Lys	Met	Thr	Leu	Gly	Met	Ile	Trp	
				115				120					125				
15	ACC	ATC	ATC	CTG	CGC	AGG	GAT	CCA	CCG	GTC	GCC	ACC	ATG	GTG	AGC	AAG	432
	Thr	Ile	Ile	Leu	Arg	Arg	Asp	Pro	Pro	Val	Ala	Thr	Met	Val	Ser	Lys	
				130				135					140				
20	GGC	GAG	GAG	CTG	TTC	ACC	GGG	GTG	GTG	CCC	ATC	CTG	GTC	GAG	CTG	GAC	480
	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	Val	Glu	Leu	Asp	
							150				155					160	
25	GGC	GAC	GTA	AAC	GGC	CAC	AAG	TTC	AGC	GTG	TCC	GGC	GAG	GGC	GAG	GGC	528
	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	Glu	Gly	Glu	Gly	
							165				170					175	
30	GAT	GCC	ACC	TAC	GGC	AAG	CTG	ACC	CTG	AAG	TTC	ATC	TGC	ACC	ACC	GGC	576
	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	Cys	Thr	Thr	Gly	
							180				185				190		
35	AAG	CTG	CCC	GTG	CCC	TGG	CCC	ACC	CTC	GTG	ACC	ACC	CTG	ACC	TAC	GGC	624
	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	Leu	Thr	Tyr	Gly	
								200					205				
40	GTG	CAG	TGC	TTC	AGC	CGC	TAC	CCC	GAC	CAC	ATG	AAG	CAG	CAC	GAC	TTC	672
	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	Gln	His	Asp	Phe	
				210				215					220				
45	TTC	AAG	TCC	GCC	ATG	CCC	GAA	GGC	TAC	GTC	CAG	GAG	CGC	ACC	ATC	TTC	720
	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	Arg	Thr	Ile	Phe	
							230				235					240	
50	TTC	AAG	GAC	GAC	GGC	AAC	TAC	AAG	ACC	CGC	GCC	GAG	GTG	AAG	TTC	GAG	768
	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	Val	Lys	Phe	Glu	
							245				250					255	
55	GGC	GAC	ACC	CTG	GTG	AAC	CGC	ATC	GAG	CTG	AAG	GGC	ATC	GAC	TTC	AAG	816
	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	Ile	Asp	Phe	Lys	
							260				265				270		
60	GAG	GAC	GGC	AAC	ATC	CTG	GGG	CAC	AAG	CTG	GAG	TAC	AAC	TAC	AAC	AGC	864
	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	Gly	Ile	Lys	Val	
							295					300					
65	AAG	TTC	AAG	ATC	GGC	GAC	AAC	ATC	GAG	CTG	AAG	GGC	ATC	GAC	TTC	AAG	912

251

Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala
 305 310 315 320
 GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG 1008
 5 Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu
 325 330 335
 CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC 1056
 10 Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro
 340 345 350
 AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC 1104
 15 Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala
 355 360 365
 GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA 1140
 Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
 370 375

20

(2) INFORMATION FOR SEQ ID NO:129:

(i) SEQUENCE CHARACTERISTICS:

25

- (A) LENGTH: 379 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

30

(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:129:

Met Asp His Tyr Asp Ser Gln Gln Thr Asn Asp Tyr Met Gln Pro Glu
 35 1 5 10 15
 Glu Asp Trp Asp Arg Asp Leu Leu Leu Asp Pro Ala Trp Glu Lys Gln
 20 25 30
 Gln Arg Lys Thr Phe Thr Ala Trp Cys Asn Ser His Leu Arg Lys Ala
 35 40 45
 40 Gly Thr Gln Ile Glu Asn Ile Glu Glu Asp Phe Arg Asp Gly Leu Lys
 50 55 60
 Leu Met Leu Leu Leu Glu Val Ile Ser Gly Glu Arg Leu Ala Lys Pro
 65 70 75 80
 Glu Arg Gly Lys Met Arg Val His Lys Ile Ser Asn Val Asn Lys Ala
 45 85 90 95
 Leu Asp Phe Ile Ala Ser Lys Gly Val Lys Leu Val Ser Ile Gly Ala
 100 105 110
 Glu Glu Ile Val Asp Gly Asn Val Lys Met Thr Leu Gly Met Ile Trp
 145 150 155 160
 Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly
 55 165 170 175
 Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly

252

		180		185		190	
	Lys	Leu	Pro	Val	Pro	Trp	Pro
		195		200		205	
5	Val	Gln	Cys	Phe	Ser	Arg	Tyr
	210		215		220		
	Phe	Lys	Ser	Ala	Met	Pro	Glu
	225		230		235		240
	Phe	Lys	Asp	Asp	Gly	Asn	Tyr
		245		250		255	
10	Gly	Asp	Thr	Leu	Val	Asn	Arg
	260		265		270		
	Glu	Asp	Gly	Asn	Ile	Leu	Gly
	275		280		285		
	His	Asn	Val	Tyr	Ile	Met	Ala
15	290		295		300		
	Asn	Phe	Lys	Ile	Arg	His	Asn
	305		310		315		320
	Asp	His	Tyr	Gln	Gln	Asn	Thr
		325		330		335	
20	Pro	Asp	Asn	His	Tyr	Leu	Ser
	340		345		350		
	Asn	Glu	Lys	Arg	Asp	His	Met
	355		360		365		
25	Gly	Ile	Thr	Leu	Gly	Met	Asp
	370		375				

(2) INFORMATION FOR SEQ ID NO:130:

(i) SEQUENCE CHARACTERISTICS:

- 30 (A) LENGTH: 3516 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- 35 (A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...3513
 40 (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:

45	ATG	GTG	AGC	AAG	GGC	GAG	GAG	CTG	TTC	ACC	GGG	GTG	GTG	CCC	ATC	CTG	48
	Met	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	
	1			5				10						15			

	CTG	GAG	CTG	GAG	GGG	GAG	CTG	AAG	GGG	GAG	AAG	CTG	AAG	CTG	TTC	GGG	36
--	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	----

	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	
	35						40					45					

55

253

	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	
	50						55					60					
5	CTG	ACC	TAC	GGC	GTG	CAG	TGC	TTC	AGC	CGC	TAC	CCC	GAC	CAC	ATG	AAG	240
	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	
	65					70				75						80	
10	CAG	CAC	GAC	TTC	TTC	AAG	TCC	GCC	ATG	CCC	GAA	GGC	TAC	GTC	CAG	GAG	288
	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	
					85					90					95		
15	CGC	ACC	ATC	TTC	TTC	AAG	GAC	GAC	GGC	AAC	TAC	AAG	ACC	CGC	GCC	GAG	336
	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	
				100					105					110			
20	GTG	AAG	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	CGC	ATC	GAG	CTG	AAG	GGC	384
	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	
			115					120					125				
25	ATC	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	CAC	AAG	CTG	GAG	TAC	432
	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	
		130					135					140					
30	AAC	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	GAC	AAG	CAG	AAG	AAC	480
	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	
	145					150				155						160	
35	GGC	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	ATC	GAG	GAC	GGC	AGC	528
	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	
					165				170						175		
40	GTG	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	CCC	ATC	GGC	GAC	GGC	576
	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	
				180				185						190			
45	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	ACC	CAG	TCC	GCC	CTG	624
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	
			195					200					205				
50	AGC	AAA	GAC	CCC	AAC	GAG	AAG	CGC	GAT	CAC	ATG	GTC	CTG	CTG	GAG	TTC	672
	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	
		210					215					220					
55	GTG	ACC	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	GAG	CTG	TAC	AAG	TCC	720
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser	
	225					230					235					240	
	CGA	CTG	AGA	TCT	CGA	GCG	ATG	AAG	CGG	CGG	GAG	CGG	GAG	CGG	GAA	CGG	768
	Asp	Gly	Gly	Asp	Ala	Pro	Gly	His	Glu	Pro	Gly	Gly	Ser	Pro	Gln	Asp	
				260					265					270			

254

	Glu	Leu	Asp	Phe	Ser	Ile	Leu	Phe	Asp	Tyr	Glu	Tyr	Leu	Asn	Pro	Asn	
			275					280					285				
5	GAA	GAA	GAG	CCG	AAT	GCA	CAT	AAG	GTC	GCC	AGC	CCA	CCC	TCC	GGA	CCC	912
	Glu	Glu	Glu	Pro	Asn	Ala	His	Lys	Val	Ala	Ser	Pro	Pro	Ser	Gly	Pro	
			290				295					300					
10	GCA	TAC	CCC	GAT	GAT	GTA	ATG	GAC	TAT	GGC	CTC	AAG	CCA	TAC	AGC	CCC	960
	Ala	Tyr	Pro	Asp	Asp	Val	Met	Asp	Tyr	Gly	Leu	Lys	Pro	Tyr	Ser	Pro	
	305					310					315					320	
15	CTT	GCT	AGT	CTC	TCT	GGC	GAG	CCC	CCC	GGC	CGA	TTC	GGA	GAG	CCG	GAT	1008
	Leu	Ala	Ser	Leu	Ser	Gly	Glu	Pro	Pro	Gly	Arg	Phe	Gly	Glu	Pro	Asp	
					325					330					335		
20	AGG	GTA	GGG	CCG	CAG	AAG	TTT	CTG	AGC	GCG	GCC	AAG	CCA	GCA	GGG	GCC	1056
	Arg	Val	Gly	Pro	Gln	Lys	Phe	Leu	Ser	Ala	Ala	Lys	Pro	Ala	Gly	Ala	
				340					345					350			
25	TCG	GGC	CTG	AGC	CCT	CGG	ATC	GAG	ATC	ACT	CCG	TCC	CAC	GAA	CTG	ATC	1104
	Ser	Gly	Leu	Ser	Pro	Arg	Ile	Glu	Ile	Thr	Pro	Ser	His	Glu	Leu	Ile	
			355					360					365				
30	CAG	GCA	GTG	GGG	CCC	CTC	CGC	ATG	AGA	GAC	GCG	GGC	CTC	CTG	GTG	GAG	1152
	Gln	Ala	Val	Gly	Pro	Leu	Arg	Met	Arg	Asp	Ala	Gly	Leu	Leu	Val	Glu	
			370				375					380					
35	CAG	CCT	CCC	CTG	GCC	GGG	GTG	GCC	GCC	AGC	CCG	AGG	TTC	ACC	CTG	CCC	1200
	Gln	Pro	Pro	Leu	Ala	Gly	Val	Ala	Ala	Ser	Pro	Arg	Phe	Thr	Leu	Pro	
	385					390					395					400	
40	GTG	CCC	GGC	TTC	GAG	GGC	TAC	CGC	GAG	CCG	CTT	TGC	TTG	AGC	CCC	GCT	1248
	Val	Pro	Gly	Phe	Glu	Gly	Tyr	Arg	Glu	Pro	Leu	Cys	Leu	Ser	Pro	Ala	
					405				410						415		
45	AGC	AGC	GGC	TCC	TCT	GCC	AGC	TTC	ATT	TCT	GAC	ACC	TTC	TCC	CCC	TAC	1296
	Ser	Ser	Gly	Ser	Ser	Ala	Ser	Phe	Ile	Ser	Asp	Thr	Phe	Ser	Pro	Tyr	
				420				425					430				
50	ACC	TCG	CCC	TGC	GTC	TCG	CCC	AAT	AAC	GGC	GGG	CCC	GAC	GAC	CTG	TGT	1344
	Thr	Ser	Pro	Cys	Val	Ser	Pro	Asn	Asn	Gly	Gly	Pro	Asp	Asp	Leu	Cys	
			435				440						445				
55	CCG	CAG	TTT	CAA	AAC	ATC	CCT	GCT	CAT	TAT	TCC	CCC	AGA	ACC	TCG	CCA	1392
	Pro	Gln	Phe	Gln	Asn	Ile	Pro	Ala	His	Tyr	Ser	Pro	Arg	Thr	Ser	Pro	
			450				455					460					
60	ATA	ATG	TCA	CCT	CGA	ACC	AGC	CTC	GCC	GAG	GAC	AGC	TGC	CTG	GGC	CGC	1440
	His	Ser	Pro	Val	Pro	Arg	Pro	Ala	Ser	Arg	Ser	Ser	Ser	Pro	Gly	Ala	
					485				490						495		
65	AAG	GGG	AGG	CAT	TGG	TGG	GCG	GAG	GCG	TTC	GTT	GGG	CTG	GCG	GCG	GCG	1488

255

	Lys	Arg	Arg	His	Ser	Cys	Ala	Glu	Ala	Leu	Val	Ala	Leu	Pro	Pro	Gly	
				500					505					510			
5	GCC	TCA	CCC	CAG	CGC	TCC	CGG	AGC	CCC	TCG	CCG	CAG	CCC	TCA	TCT	CAC	1584
	Ala	Ser	Pro	Gln	Arg	Ser	Arg	Ser	Pro	Ser	Pro	Gln	Pro	Ser	Ser	His	
			515					520					525				
10	GTG	GCA	CCC	CAG	GAC	CAC	GGC	TCC	CCG	GCT	GGG	TAC	CCC	CCT	GTG	GCT	1632
	Val	Ala	Pro	Gln	Asp	His	Gly	Ser	Pro	Ala	Gly	Tyr	Pro	Pro	Val	Ala	
			530				535					540					
15	GGC	TCT	GCC	GTG	ATC	ATG	GAT	GCC	CTG	AAC	AGC	CTC	GCC	ACG	GAC	TCG	1680
	Gly	Ser	Ala	Val	Ile	Met	Asp	Ala	Leu	Asn	Ser	Leu	Ala	Thr	Asp	Ser	
	545					550					555					560	
	CCT	TGT	GGG	ATC	CCC	CCC	AAG	ATG	TGG	AAG	ACC	AGC	CCT	GAC	CCC	TCG	1728
	Pro	Cys	Gly	Ile	Pro	Pro	Lys	Met	Trp	Lys	Thr	Ser	Pro	Asp	Pro	Ser	
					565					570					575		
20	CCG	GTG	TCT	GCC	GCC	CCA	TCC	AAG	GCC	GGC	CTG	CCT	CGC	CAC	ATC	TAC	1776
	Pro	Val	Ser	Ala	Ala	Pro	Ser	Lys	Ala	Gly	Leu	Pro	Arg	His	Ile	Tyr	
				580					585					590			
25	CCG	GCC	GTG	GAG	TTC	CTG	GGG	CCC	TGC	GAG	CAG	GGC	GAG	AGG	AGA	AAC	1824
	Pro	Ala	Val	Glu	Phe	Leu	Gly	Pro	Cys	Glu	Gln	Gly	Glu	Arg	Arg	Asn	
			595				600						605				
30	TCG	GCT	CCA	GAA	TCC	ATC	CTG	CTG	GTT	CCG	CCC	ACT	TGG	CCC	AAG	CCG	1872
	Ser	Ala	Pro	Glu	Ser	Ile	Leu	Leu	Val	Pro	Pro	Thr	Trp	Pro	Lys	Pro	
			610				615						620				
35	CTG	GTG	CCT	GCC	ATT	CCC	ATC	TGC	AGC	ATC	CCA	GTG	ACT	GCA	TCC	CTC	1920
	Leu	Val	Pro	Ala	Ile	Pro	Ile	Cys	Ser	Ile	Pro	Val	Thr	Ala	Ser	Leu	
	625					630					635					640	
	CCT	CCA	CTT	GAG	TGG	CCG	CTG	TCC	AGT	CAG	TCA	GGC	TCT	TAC	GAG	CTG	1968
	Pro	Pro	Leu	Glu	Trp	Pro	Leu	Ser	Ser	Gln	Ser	Gly	Ser	Tyr	Glu	Leu	
					645					650					655		
40	CGG	ATC	GAG	GTG	CAG	CCC	AAG	CCA	CAT	CAC	CGG	GCC	CAC	TAT	GAG	ACA	2016
	Arg	Ile	Glu	Val	Gln	Pro	Lys	Pro	His	His	Arg	Ala	His	Tyr	Glu	Thr	
				660					665					670			
45	GAA	GGC	AGC	CGA	GGG	GCT	GTC	AAA	GCT	CCA	ACT	GGA	GGC	CAC	CCT	GTG	2064
	Glu	Gly	Ser	Arg	Gly	Ala	Val	Lys	Ala	Pro	Thr	Gly	Gly	His	Pro	Val	
			675					680					685				
55	GTT	CAG	CTC	CAT	GGC	TAC	ATG	GAA	AAC	AAG	CCT	CTG	GCG	GTT	CAG	ATC	2112
	Phe	Ile	Gly	Thr	Ala	Asp	Glu	Arg	Ile	Leu	Lys	Pro	His	Ala	Phe	Tyr	
	705					710					715					720	
	CAG	GTG	CAG	CGA	ATG	AGC	GGC	AAA	GCT	CCA	ACT	GGA	GGC	CAC	CCT	GTG	

256

	Gln	Val	His	Arg	Ile	Thr	Gly	Lys	Thr	Val	Thr	Thr	Thr	Ser	Tyr	Glu	
					725					730						735	
5	AAG	ATA	GTG	GGC	AAC	ACC	AAA	GTC	CTG	GAG	ATC	CCC	TTG	GAG	CCC	AAA	2256
	Lys	Ile	Val	Gly	Asn	Thr	Lys	Val	Leu	Glu	Ile	Pro	Leu	Glu	Pro	Lys	
				740					745					750			
10	AAC	AAC	ATG	AGG	GCA	ACC	ATC	GAC	TGT	GCG	GGG	ATC	TTG	AAG	CTT	AGA	2304
	Asn	Asn	Met	Arg	Ala	Thr	Ile	Asp	Cys	Ala	Gly	Ile	Leu	Lys	Leu	Arg	
			755					760					765				
15	AAC	GCC	GAC	ATT	GAG	CTG	CGG	AAA	GGC	GAG	ACG	GAC	ATT	GGA	AGA	AAG	2352
	Asn	Ala	Asp	Ile	Glu	Leu	Arg	Lys	Gly	Glu	Thr	Asp	Ile	Gly	Arg	Lys	
		770					775					780					
	AAC	ACG	CGG	GTG	AGA	CTG	GTT	TTC	CGA	GTT	CAC	ATC	CCA	GAG	TCC	AGT	2400
	Asn	Thr	Arg	Val	Arg	Leu	Val	Phe	Arg	Val	His	Ile	Pro	Glu	Ser	Ser	
	785					790					795					800	
20	GGC	AGA	ATC	GTC	TCT	TTA	CAG	ACT	GCA	TCT	AAC	CCC	ATC	GAG	TGC	TCC	2448
	Gly	Arg	Ile	Val	Ser	Leu	Gln	Thr	Ala	Ser	Asn	Pro	Ile	Glu	Cys	Ser	
					805					810					815		
25	CAG	CGA	TCT	GCT	CAC	GAG	CTG	CCC	ATG	GTT	GAA	AGA	CAA	GAC	ACA	GAC	2496
	Gln	Arg	Ser	Ala	His	Glu	Leu	Pro	Met	Val	Glu	Arg	Gln	Asp	Thr	Asp	
				820					825					830			
30	AGC	TGC	CTG	GTC	TAT	GGC	GGC	CAG	CAA	ATG	ATC	CTC	ACG	GGG	CAG	AAC	2544
	Ser	Cys	Leu	Val	Tyr	Gly	Gly	Gln	Gln	Met	Ile	Leu	Thr	Gly	Gln	Asn	
			835					840					845				
35	TTT	ACA	TCC	GAG	TCC	AAA	GTT	GTG	TTT	ACT	GAG	AAG	ACC	ACA	GAT	GGA	2592
	Phe	Thr	Ser	Glu	Ser	Lys	Val	Val	Phe	Thr	Glu	Lys	Thr	Thr	Asp	Gly	
		850					855					860					
	CAG	CAA	ATT	TGG	GAG	ATG	GAA	GCC	ACG	GTG	GAT	AAG	GAC	AAG	AGC	CAG	2640
	Gln	Gln	Ile	Trp	Glu	Met	Glu	Ala	Thr	Val	Asp	Lys	Asp	Lys	Ser	Gln	
	865					870					875					880	
40	CCC	AAC	ATG	CTT	TTT	GTT	GAG	ATC	CCT	GAA	TAT	CGG	AAC	AAG	CAT	ATC	2688
	Pro	Asn	Met	Leu	Phe	Val	Glu	Ile	Pro	Glu	Tyr	Arg	Asn	Lys	His	Ile	
					885					890					895		
45	CGC	ACA	CCT	GTA	AAA	GTG	AAC	TTC	TAC	GTC	ATC	AAT	GGG	AAG	AGA	AAA	2736
	Arg	Thr	Pro	Val	Lys	Val	Asn	Phe	Tyr	Val	Ile	Asn	Gly	Lys	Arg	Lys	
				900					905					910			
55	Thr	Glu	Pro	Thr	Asp	Glu	Tyr	Asp	Pro	Thr	Leu	Ile	Cys	Ser	Pro	Thr	
		930						935					940				

257

	His Gly Gly Leu Gly Ser Gln Pro Tyr Tyr Pro Gln His Pro Met Val	
	945 950 955 960	
5	GCC GAG TCC CCC TCC TGC CTC GTG GCC ACC ATG GCT CCC TGC CAG CAG Ala Glu Ser Pro Ser Cys Leu Val Ala Thr Met Ala Pro Cys Gln Gln	2928
	965 970 975	
10	TTC CGC ACG GGG CTC TCA TCC CCT GAC GCC CGC TAC CAG CAA CAG AAC Phe Arg Thr Gly Leu Ser Ser Pro Asp Ala Arg Tyr Gln Gln Gln Asn	2976
	980 985 990	
15	CCA GCG GCC GTA CTC TAC CAG CGG AGC AAG AGC CTG AGC CCC AGC CTG Pro Ala Ala Val Leu Tyr Gln Arg Ser Lys Ser Leu Ser Pro Ser Leu	3024
	995 1000 1005	
	CTG GGC TAT CAG CAG CCG GCC CTC ATG GCC GCC CCG CTG TCC CTT GCG Leu Gly Tyr Gln Gln Pro Ala Leu Met Ala Ala Pro Leu Ser Leu Ala	3072
	1010 1015 1020	
20	GAC GCT CAC CGC TCT GTG CTG GTG CAC GCC GGC TCC CAG GGC CAG AGC Asp Ala His Arg Ser Val Leu Val His Ala Gly Ser Gln Gly Gln Ser	3120
	1025 1030 1035 1040	
25	TCA GCC CTG CTC CAC CCC TCT CCG ACC AAC CAG CAG GCC TCG CCT GTG Ser Ala Leu Leu His Pro Ser Pro Thr Asn Gln Gln Ala Ser Pro Val	3168
	1045 1050 1055	
30	ATC CAC TAC TCA CCC ACC AAC CAG CAG CTG CGC TGC GGA AGC CAC CAG Ile His Tyr Ser Pro Thr Asn Gln Gln Leu Arg Cys Gly Ser His Gln	3216
	1060 1065 1070	
35	GAG TTC CAG CAC ATC ATG TAC TGC GAG AAT TTC GCA CCA GGC ACC ACC Glu Phe Gln His Ile Met Tyr Cys Glu Asn Phe Ala Pro Gly Thr Thr	3264
	1075 1080 1085	
	AGA CCT GGC CCG CCC CCG GTC AGT CAA GGT CAG AGG CTG AGC CCG GGT Arg Pro Gly Pro Pro Pro Val Ser Gln Gly Gln Arg Leu Ser Pro Gly	3312
	1090 1095 1100	
40	TCC TAC CCC ACA GTC ATT CAG CAG CAG AAT GCC ACG AGC CAA AGA GCC Ser Tyr Pro Thr Val Ile Gln Gln Gln Asn Ala Thr Ser Gln Arg Ala	3360
	1105 1110 1115 1120	
45	GCC AAA AAC GGA CCC CCG GTC AGT GAC CAA AAG GAA GTA TTA CCT GCG Ala Lys Asn Gly Pro Pro Val Ser Asp Gln Lys Glu Val Leu Pro Ala	3408
	1125 1130 1135	
	CCC CTC ACC ATT ACC GCG GCG GCG ACC TCC ACC ACC ACC ACC ACC	
	1140 1145 1150 1155 1160 1165	
55	Asp Val Asn Glu Ile Ile Arg Lys Glu Phe Ser Gly Pro Pro Ala Arg	
	1155 1160 1165	

258

Asn Gln Thr
1170

5 (2) INFORMATION FOR SEQ ID NO:131:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1171 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:131:

	Met	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu
	1				5					10					15	
20	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly
				20					25					30		
	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile
				35				40						45		
	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr
25		50					55					60				
	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys
	65					70					75					80
	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu
					85					90					95	
30	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu
				100					105					110		
	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly
				115				120					125			
	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr
35		130					135					140				
	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn
	145					150					155					160
	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser
					165				170						175	
40	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly
				180					185					190		
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu
				195				200					205			
	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe
45		210					215					220				
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser
	225					230					235					240
	Glu	Ile	Arg	Ser	Leu	Ile	Met	Leu	Ile	Phe	Gln	Leu	Gly	Pro	Gln	Pro

	1977-1978				1978-1979				1979-1980				1980-1981			
	275				280				285							
55	Glu	Glu	Glu	Pro	Asn	Ala	His	Lys	Val	Ala	Ser	Pro	Pro	Ser	Gly	Pro
	290					295						300				

259

305 310 315 320
 Leu Ala Ser Leu Ser Gly Glu Pro Pro Gly Arg Phe Gly Glu Pro Asp
 325 330 335
 Arg Val Gly Pro Gln Lys Phe Leu Ser Ala Ala Lys Pro Ala Gly Ala
 340 345 350
 5 Ser Gly Leu Ser Pro Arg Ile Glu Ile Thr Pro Ser His Glu Leu Ile
 355 360 365
 Gln Ala Val Gly Pro Leu Arg Met Arg Asp Ala Gly Leu Leu Val Glu
 370 375 380
 10 Gln Pro Pro Leu Ala Gly Val Ala Ala Ser Pro Arg Phe Thr Leu Pro
 385 390 395 400
 Val Pro Gly Phe Glu Gly Tyr Arg Glu Pro Leu Cys Leu Ser Pro Ala
 405 410 415
 Ser Ser Gly Ser Ala Ser Phe Ile Ser Asp Thr Phe Ser Pro Tyr
 420 425 430
 15 Thr Ser Pro Cys Val Ser Pro Asn Asn Gly Gly Pro Asp Asp Leu Cys
 435 440 445
 Pro Gln Phe Gln Asn Ile Pro Ala His Tyr Ser Pro Arg Thr Ser Pro
 450 455 460
 20 Ile Met Ser Pro Arg Thr Ser Leu Ala Glu Asp Ser Cys Leu Gly Arg
 465 470 475 480
 His Ser Pro Val Pro Arg Pro Ala Ser Arg Ser Ser Ser Pro Gly Ala
 485 490 495
 Lys Arg Arg His Ser Cys Ala Glu Ala Leu Val Ala Leu Pro Pro Gly
 500 505 510
 25 Ala Ser Pro Gln Arg Ser Arg Ser Pro Ser Pro Gln Pro Ser Ser His
 515 520 525
 Val Ala Pro Gln Asp His Gly Ser Pro Ala Gly Tyr Pro Pro Val Ala
 530 535 540
 30 Gly Ser Ala Val Ile Met Asp Ala Leu Asn Ser Leu Ala Thr Asp Ser
 545 550 555 560
 Pro Cys Gly Ile Pro Pro Lys Met Trp Lys Thr Ser Pro Asp Pro Ser
 565 570 575
 Pro Val Ser Ala Ala Pro Ser Lys Ala Gly Leu Pro Arg His Ile Tyr
 580 585 590
 35 Pro Ala Val Glu Phe Leu Gly Pro Cys Glu Gln Gly Glu Arg Arg Asn
 595 600 605
 Ser Ala Pro Glu Ser Ile Leu Leu Val Pro Pro Thr Trp Pro Lys Pro
 610 615 620
 40 Leu Val Pro Ala Ile Pro Ile Cys Ser Ile Pro Val Thr Ala Ser Leu
 625 630 635 640
 Pro Pro Leu Glu Trp Pro Leu Ser Ser Gln Ser Gly Ser Tyr Glu Leu
 645 650 655
 Arg Ile Glu Val Gln Pro Lys Pro His His Arg Ala His Tyr Glu Thr
 660 665 670
 45 Glu Gly Ser Arg Gly Ala Val Lys Ala Pro Thr Gly Gly His Pro Val
 675 680 685
 Val Gln Ser His Glu Thr Met Gln Thr Thr Pro Leu Glu Thr Glu Thr
 690 695 700
 50 Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr
 705 710 715 720 725 730 735
 Lys Ile Val Gly Asn Thr Lys Val Leu Glu Ile Pro Leu Glu Pro Lys
 740 745 750
 Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr
 755 760 765 770 775 780 785 790 795 800

260

		755				760						765					
		Asn	Ala	Asp	Ile	Glu	Leu	Arg	Lys	Gly	Glu	Thr	Asp	Ile	Gly	Arg	Lys
		770						775					780				
5		Asn	Thr	Arg	Val	Arg	Leu	Val	Phe	Arg	Val	His	Ile	Pro	Glu	Ser	Ser
		785					790					795				800	
		Gly	Arg	Ile	Val	Ser	Leu	Gln	Thr	Ala	Ser	Asn	Pro	Ile	Glu	Cys	Ser
						805						810				815	
		Gln	Arg	Ser	Ala	His	Glu	Leu	Pro	Met	Val	Glu	Arg	Gln	Asp	Thr	Asp
					820					825					830		
10		Ser	Cys	Leu	Val	Tyr	Gly	Gly	Gln	Gln	Met	Ile	Leu	Thr	Gly	Gln	Asn
				835					840						845		
		Phe	Thr	Ser	Glu	Ser	Lys	Val	Val	Phe	Thr	Glu	Lys	Thr	Thr	Asp	Gly
				850				855					860				
		Gln	Gln	Ile	Trp	Glu	Met	Glu	Ala	Thr	Val	Asp	Lys	Asp	Lys	Ser	Gln
15		865				870						875				880	
		Pro	Asn	Met	Leu	Phe	Val	Glu	Ile	Pro	Glu	Tyr	Arg	Asn	Lys	His	Ile
					885						890					895	
		Arg	Thr	Pro	Val	Lys	Val	Asn	Phe	Tyr	Val	Ile	Asn	Gly	Lys	Arg	Lys
					900					905					910		
20		Arg	Ser	Gln	Pro	Gln	His	Phe	Thr	Tyr	His	Pro	Val	Pro	Ala	Ile	Lys
				915					920						925		
		Thr	Glu	Pro	Thr	Asp	Glu	Tyr	Asp	Pro	Thr	Leu	Ile	Cys	Ser	Pro	Thr
				930				935					940				
		His	Gly	Gly	Leu	Gly	Ser	Gln	Pro	Tyr	Tyr	Pro	Gln	His	Pro	Met	Val
25		945				950						955				960	
		Ala	Glu	Ser	Pro	Ser	Cys	Leu	Val	Ala	Thr	Met	Ala	Pro	Cys	Gln	Gln
					965						970					975	
		Phe	Arg	Thr	Gly	Leu	Ser	Ser	Pro	Asp	Ala	Arg	Tyr	Gln	Gln	Gln	Asn
					980					985					990		
30		Pro	Ala	Ala	Val	Leu	Tyr	Gln	Arg	Ser	Lys	Ser	Leu	Ser	Pro	Ser	Leu
				995					1000						1005		
		Leu	Gly	Tyr	Gln	Gln	Pro	Ala	Leu	Met	Ala	Ala	Pro	Leu	Ser	Leu	Ala
				1010				1015					1020				
		Asp	Ala	His	Arg	Ser	Val	Leu	Val	His	Ala	Gly	Ser	Gln	Gly	Gln	Ser
35		025				1030						1035				1040	
		Ser	Ala	Leu	Leu	His	Pro	Ser	Pro	Thr	Asn	Gln	Gln	Ala	Ser	Pro	Val
					1045						1050					1055	
		Ile	His	Tyr	Ser	Pro	Thr	Asn	Gln	Gln	Leu	Arg	Cys	Gly	Ser	His	Gln
				1060					1065						1070		
40		Glu	Phe	Gln	His	Ile	Met	Tyr	Cys	Glu	Asn	Phe	Ala	Pro	Gly	Thr	Thr
				1075					1080						1085		
		Arg	Pro	Gly	Pro	Pro	Pro	Val	Ser	Gln	Gly	Gln	Arg	Leu	Ser	Pro	Gly
				1090				1095					1100				
		Ser	Tyr	Pro	Thr	Val	Ile	Gln	Gln	Gln	Asn	Ala	Thr	Ser	Gln	Arg	Ala
45		105				1110						1115				1120	
		Ala	Lys	Asn	Gly	Pro	Pro	Val	Ser	Asp	Gln	Lys	Glu	Val	Leu	Pro	Ala
					1125						1130					1135	
		Gly	Val	Thr	Ile	Lys	Gln	Gln	Gln	Asn	Leu	Thr	Gln	Thr	Thr	Thr	Thr

1170

55

(2) INFORMATION FOR SEQ ID NO:132:

261

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 3546 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
 (ix) FEATURE:

(A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...3543
 (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:

15	ATG AAC GCC CCC GAG CGG CAG CCC CAA CCC GAC GGC GGG GAC GCC CCA	48
	Met Asn Ala Pro Glu Arg Gln Pro Gln Pro Asp Gly Gly Asp Ala Pro	
	1 5 10 15	
20	GGC CAC GAG CCT GGG GGC AGC CCC CAA GAC GAG CTT GAC TTC TCC ATC	96
	Gly His Glu Pro Gly Gly Ser Pro Gln Asp Glu Leu Asp Phe Ser Ile	
	20 25 30	
25	CTC TTC GAC TAT GAG TAT TTG AAT CCG AAC GAA GAA GAG CCG AAT GCA	144
	Leu Phe Asp Tyr Glu Tyr Leu Asn Pro Asn Glu Glu Pro Asn Ala	
	35 40 45	
30	CAT AAG GTC GCC AGC CCA CCC TCC GGA CCC GCA TAC CCC GAT GAT GTA	192
	His Lys Val Ala Ser Pro Pro Ser Gly Pro Ala Tyr Pro Asp Asp Val	
	50 55 60	
35	ATG GAC TAT GGC CTC AAG CCA TAC AGC CCC CTT GCT AGT CTC TCT GGC	240
	Met Asp Tyr Gly Leu Lys Pro Tyr Ser Pro Leu Ala Ser Leu Ser Gly	
	65 70 75 80	
40	GAG CCC CCC GGC CGA TTC GGA GAG CCG GAT AGG GTA GGG CCG CAG AAG	288
	Glu Pro Pro Gly Arg Phe Gly Glu Pro Asp Arg Val Gly Pro Gln Lys	
	85 90 95	
45	TTT CTG AGC GCG GCC AAG CCA GCA GGG GCC TCG GGC CTG AGC CCT CGG	336
	Phe Leu Ser Ala Ala Lys Pro Ala Gly Ala Ser Gly Leu Ser Pro Arg	
	100 105 110	
50	ATC GAG ATC ACT CCG TCC CAC GAA CTG ATC CAG GCA GTG GGG CCC CTC	384
	Ile Glu Ile Thr Pro Ser His Glu Leu Ile Gln Ala Val Gly Pro Leu	
	115 120 125	
55	GGC ATG AGA GAC GCG GCG CTC CTC CTC GAG GAG GGT GCG CTC GCG GCG	432
	Val Ala Ala Ser Pro Arg Phe Thr Leu Pro Val Pro Gly Phe Glu Gly	
	145 150 155 160	

262

	Tyr	Arg	Glu	Pro	Leu	Cys	Leu	Ser	Pro	Ala	Ser	Ser	Gly	Ser	Ser	Ala	
					165					170						175	
5	AGC	TTC	ATT	TCT	GAC	ACC	TTC	TCC	CCC	TAC	ACC	TCG	CCC	TGC	GTC	TCG	576
	Ser	Phe	Ile	Ser	Asp	Thr	Phe	Ser	Pro	Tyr	Thr	Ser	Pro	Cys	Val	Ser	
				180					185					190			
10	CCC	AAT	AAC	GGC	GGG	CCC	GAC	GAC	CTG	TGT	CCG	CAG	TTT	CAA	AAC	ATC	624
	Pro	Asn	Asn	Gly	Gly	Pro	Asp	Asp	Leu	Cys	Pro	Gln	Phe	Gln	Asn	Ile	
			195					200					205				
15	CCT	GCT	CAT	TAT	TCC	CCC	AGA	ACC	TCG	CCA	ATA	ATG	TCA	CCT	CGA	ACC	672
	Pro	Ala	His	Tyr	Ser	Pro	Arg	Thr	Ser	Pro	Ile	Met	Ser	Pro	Arg	Thr	
		210					215					220					
20	AGC	CTC	GCC	GAG	GAC	AGC	TGC	CTG	GGC	CGC	CAC	TCG	CCC	GTG	CCC	CGT	720
	Ser	Leu	Ala	Glu	Asp	Ser	Cys	Leu	Gly	Arg	His	Ser	Pro	Val	Pro	Arg	
	225					230				235						240	
25	CCG	GCC	TCC	CGC	TCC	TCA	TCG	CCT	GGT	GCC	AAG	CGG	AGG	CAT	TCG	TGC	768
	Pro	Ala	Ser	Arg	Ser	Ser	Ser	Pro	Gly	Ala	Lys	Arg	Arg	His	Ser	Cys	
					245					250					255		
30	GCC	GAG	GCC	TTG	GTT	GCC	CTG	CCG	CCC	GGA	GCC	TCA	CCC	CAG	CGC	TCC	816
	Ala	Glu	Ala	Leu	Val	Ala	Leu	Pro	Pro	Gly	Ala	Ser	Pro	Gln	Arg	Ser	
				260					265					270			
35	CGG	AGC	CCC	TCG	CCG	CAG	CCC	TCA	TCT	CAC	GTG	GCA	CCC	CAG	GAC	CAC	864
	Arg	Ser	Pro	Ser	Pro	Gln	Pro	Ser	Ser	His	Val	Ala	Pro	Gln	Asp	His	
			275					280					285				
40	GGC	TCC	CCG	GCT	GGG	TAC	CCC	CCT	GTG	GCT	GGC	TCT	GCC	GTG	ATC	ATG	912
	Gly	Ser	Pro	Ala	Gly	Tyr	Pro	Pro	Val	Ala	Gly	Ser	Ala	Val	Ile	Met	
		290					295					300					
45	GAT	GCC	CTG	AAC	AGC	CTC	GCC	ACG	GAC	TCG	CCT	TGT	GGG	ATC	CCC	CCC	960
	Asp	Ala	Leu	Asn	Ser	Leu	Ala	Thr	Asp	Ser	Pro	Cys	Gly	Ile	Pro	Pro	
	305					310				315					320		
50	AAG	ATG	TGG	AAG	ACC	AGC	CCT	GAC	CCC	TCG	CCG	GTG	TCT	GCC	GCC	CCA	1008
	Lys	Met	Trp	Lys	Thr	Ser	Pro	Asp	Pro	Ser	Pro	Val	Ser	Ala	Ala	Pro	
					325				330					335			
55	TCC	AAG	GCC	GGC	CTG	CCT	CGC	CAC	ATC	TAC	CCG	GCC	GTG	GAG	TTC	CTG	1056
	Ser	Lys	Ala	Gly	Leu	Pro	Arg	His	Ile	Tyr	Pro	Ala	Val	Glu	Phe	Leu	
				340				345					350				
	GGG	CCC	TCC	GAC	CAG	CCC	GAG	ACC	TCG	CCG	GTG	TCT	GCC	GCC	CCA		
	Leu	Leu	Val	Pro	Pro	Thr	Trp	Pro	Lys	Pro	Leu	Val	Pro	Ala	Ile	Pro	
			370				375				380						

263

	Ile	Cys	Ser	Ile	Pro	Val	Thr	Ala	Ser	Leu	Pro	Pro	Leu	Glu	Trp	Pro	
	385					390					395					400	
5	CTG	TCC	AGT	CAG	TCA	GGC	TCT	TAC	GAG	CTG	CGG	ATC	GAG	GTG	CAG	CCC	1248
	Leu	Ser	Ser	Gln	Ser	Gly	Ser	Tyr	Glu	Leu	Arg	Ile	Glu	Val	Gln	Pro	
				405					410						415		
10	AAG	CCA	CAT	CAC	CGG	GCC	CAC	TAT	GAG	ACA	GAA	GGC	AGC	CGA	GGG	GCT	1296
	Lys	Pro	His	His	Arg	Ala	His	Tyr	Glu	Thr	Glu	Gly	Ser	Arg	Gly	Ala	
				420					425					430			
15	GTC	AAA	GCT	CCA	ACT	GGA	GGC	CAC	CCT	GTG	GTT	CAG	CTC	CAT	GGC	TAC	1344
	Val	Lys	Ala	Pro	Thr	Gly	Gly	His	Pro	Val	Val	Gln	Leu	His	Gly	Tyr	
			435					440					445				
20	ATG	GAA	AAC	AAG	CCT	CTG	GGA	CTT	CAG	ATC	TTC	ATT	GGG	ACA	GCT	GAT	1392
	Met	Glu	Asn	Lys	Pro	Leu	Gly	Leu	Gln	Ile	Phe	Ile	Gly	Thr	Ala	Asp	
		450					455					460					
25	GAG	CGG	ATC	CTT	AAG	CCG	CAC	GCC	TTC	TAC	CAG	GTG	CAC	CGA	ATC	ACG	1440
	Glu	Arg	Ile	Leu	Lys	Pro	His	Ala	Phe	Tyr	Gln	Val	His	Arg	Ile	Thr	
		465				470					475					480	
30	GGG	AAA	ACT	GTC	ACC	ACC	ACC	AGC	TAT	GAG	AAG	ATA	GTG	GGC	AAC	ACC	1488
	Gly	Lys	Thr	Val	Thr	Thr	Thr	Ser	Tyr	Glu	Lys	Ile	Val	Gly	Asn	Thr	
				485						490					495		
35	AAA	GTC	CTG	GAG	ATC	CCC	TTG	GAG	CCC	AAA	AAC	AAC	ATG	AGG	GCA	ACC	1536
	Lys	Val	Leu	Glu	Ile	Pro	Leu	Glu	Pro	Lys	Asn	Asn	Met	Arg	Ala	Thr	
			500						505					510			
40	ATC	GAC	TGT	GCG	GGG	ATC	TTG	AAG	CTT	AGA	AAC	GCC	GAC	ATT	GAG	CTG	1584
	Ile	Asp	Cys	Ala	Gly	Ile	Leu	Lys	Leu	Arg	Asn	Ala	Asp	Ile	Glu	Leu	
			515					520					525				
45	CGG	AAA	GGC	GAG	ACG	GAC	ATT	GGA	AGA	AAG	AAC	ACG	CGG	GTG	AGA	CTG	1632
	Arg	Lys	Gly	Glu	Thr	Asp	Ile	Gly	Arg	Lys	Asn	Thr	Arg	Val	Arg	Leu	
		530					535					540					
50	GTT	TTC	CGA	GTT	CAC	ATC	CCA	GAG	TCC	AGT	GGC	AGA	ATC	GTC	TCT	TTA	1680
	Val	Phe	Arg	Val	His	Ile	Pro	Glu	Ser	Ser	Gly	Arg	Ile	Val	Ser	Leu	
		545				550					555					560	
55	CAG	ACT	GCA	TCT	AAC	CCC	ATC	GAG	TGC	TCC	CAG	CGA	TCT	GCT	CAC	GAG	1728
	Gln	Thr	Ala	Ser	Asn	Pro	Ile	Glu	Cys	Ser	Gln	Arg	Ser	Ala	His	Glu	
				565					570						575		
60	GGG	CAG	CAA	ATG	ATC	CTC	ACG	GGG	CAG	AAC	TTT	ACA	TCC	GAG	TCC	AAA	1824
	Gly	Gln	Gln	Met	Ile	Leu	Thr	Gly	Gln	Asn	Phe	Thr	Ser	Glu	Ser	Lys	
			595					600					605				

264

	Val	Val	Phe	Thr	Glu	Lys	Thr	Thr	Asp	Gly	Gln	Gln	Ile	Trp	Glu	Met	
	610						615					620					
5	GAA	GCC	ACG	GTG	GAT	AAG	GAC	AAG	AGC	CAG	CCC	AAC	ATG	CTT	TTT	GTT	1920
	Glu	Ala	Thr	Val	Asp	Lys	Asp	Lys	Ser	Gln	Pro	Asn	Met	Leu	Phe	Val	
	625					630					635					640	
10	GAG	ATC	CCT	GAA	TAT	CGG	AAC	AAG	CAT	ATC	CGC	ACA	CCT	GTA	AAA	GTG	1968
	Glu	Ile	Pro	Glu	Tyr	Arg	Asn	Lys	His	Ile	Arg	Thr	Pro	Val	Lys	Val	
					645					650						655	
15	AAC	TTC	TAC	GTC	ATC	AAT	GGG	AAG	AGA	AAA	CGA	AGT	CAG	CCT	CAG	CAC	2016
	Asn	Phe	Tyr	Val	Ile	Asn	Gly	Lys	Arg	Lys	Arg	Ser	Gln	Pro	Gln	His	
				660					665						670		
20	TTT	ACC	TAC	CAC	CCA	GTC	CCA	GCC	ATC	AAG	ACG	GAG	CCC	ACG	GAT	GAA	2064
	Phe	Thr	Tyr	His	Pro	Val	Pro	Ala	Ile	Lys	Thr	Glu	Pro	Thr	Asp	Glu	
				675				680						685			
25	TAT	GAC	CCC	ACT	CTG	ATC	TGC	AGC	CCC	ACC	CAT	GGA	GGC	CTG	GGG	AGC	2112
	Tyr	Asp	Pro	Thr	Leu	Ile	Cys	Ser	Pro	Thr	His	Gly	Gly	Leu	Gly	Ser	
		690					695					700					
30	CAG	CCT	TAC	TAC	CCC	CAG	CAC	CCG	ATG	GTG	GCC	GAG	TCC	CCC	TCC	TGC	2160
	Gln	Pro	Tyr	Tyr	Pro	Gln	His	Pro	Met	Val	Ala	Glu	Ser	Pro	Ser	Cys	
	705					710					715					720	
35	CTC	GTG	GCC	ACC	ATG	GCT	CCC	TGC	CAG	CAG	TTC	CGC	ACG	GGG	CTC	TCA	2208
	Leu	Val	Ala	Thr	Met	Ala	Pro	Cys	Gln	Gln	Phe	Arg	Thr	Gly	Leu	Ser	
					725					730					735		
40	TCC	CCT	GAC	GCC	CGC	TAC	CAG	CAA	CAG	AAC	CCA	GCG	GCC	GTA	CTC	TAC	2256
	Ser	Pro	Asp	Ala	Arg	Tyr	Gln	Gln	Gln	Asn	Pro	Ala	Ala	Val	Leu	Tyr	
				740					745					750			
45	CAG	CGG	AGC	AAG	AGC	CTG	AGC	CCC	AGC	CTG	CTG	GGC	TAT	CAG	CAG	CCG	2304
	Gln	Arg	Ser	Lys	Ser	Leu	Ser	Pro	Ser	Leu	Leu	Gly	Tyr	Gln	Gln	Pro	
			755					760					765				
50	GCC	CTC	ATG	GCC	GCC	CCG	CTG	TCC	CTT	GCG	GAC	GCT	CAC	CGC	TCT	GTG	2352
	Ala	Leu	Met	Ala	Ala	Pro	Leu	Ser	Leu	Ala	Asp	Ala	His	Arg	Ser	Val	
		770					775					780					
55	CTG	GTG	CAC	GCC	GGC	TCC	CAG	GGC	CAG	AGC	TCA	GCC	CTG	CTC	CAC	CCC	2400
	Leu	Val	His	Ala	Gly	Ser	Gln	Gly	Gln	Ser	Ser	Ala	Leu	Leu	His	Pro	
	785					790					795					800	
60	AAC	CAG	CAG	CTG	CCG	TCC	CGA	AGC	CAC	CAG	GAG	TTC	CAG	CAC	ATC	ATC	2448
	Asn	Gln	Gln	Leu	Arg	Cys	Gly	Ser	His	Gln	Glu	Phe	Gln	His	Ile	Met	
				820					825					830			

265

	Tyr	Cys	Glu	Asn	Phe	Ala	Pro	Gly	Thr	Thr	Arg	Pro	Gly	Pro	Pro	Pro	
			835					840					845				
5	GTC	AGT	CAA	GGT	CAG	AGG	CTG	AGC	CCG	GGT	TCC	TAC	CCC	ACA	GTC	ATT	2592
	Val	Ser	Gln	Gly	Gln	Arg	Leu	Ser	Pro	Gly	Ser	Tyr	Pro	Thr	Val	Ile	
			850				855					860					
10	CAG	CAG	CAG	AAT	GCC	ACG	AGC	CAA	AGA	GCC	GCC	AAA	AAC	GGA	CCC	CCG	2640
	Gln	Gln	Gln	Asn	Ala	Thr	Ser	Gln	Arg	Ala	Lys	Asn	Gly	Pro	Pro		
			865			870					875				880		
15	GTC	AGT	GAC	CAA	AAG	GAA	GTA	TTA	CCT	GCG	GGG	GTG	ACC	ATT	AAA	CAG	2688
	Val	Ser	Asp	Gln	Lys	Glu	Val	Leu	Pro	Ala	Gly	Val	Thr	Ile	Lys	Gln	
					885					890				895			
	GAG	CAG	AAC	TTG	GAC	CAG	ACC	TAC	TTG	GAT	GAT	GTT	AAT	GAA	ATT	ATC	2736
	Glu	Gln	Asn	Leu	Asp	Gln	Thr	Tyr	Leu	Asp	Asp	Val	Asn	Glu	Ile	Ile	
				900					905				910				
20	AGG	AAG	GAG	TTT	TCA	GGA	CCT	CCT	GCC	AGA	AAT	CAG	ACG	AGA	ATT	CTG	2784
	Arg	Lys	Glu	Phe	Ser	Gly	Pro	Pro	Ala	Arg	Asn	Gln	Thr	Arg	Ile	Leu	
			915				920					925					
25	CAG	TCG	ACG	GTA	CCG	CGG	GCC	CGG	GAT	CCA	CCG	GTC	GCC	ACC	ATG	GTG	2832
	Gln	Ser	Thr	Val	Pro	Arg	Ala	Arg	Asp	Pro	Pro	Val	Ala	Thr	Met	Val	
		930				935						940					
30	AGC	AAG	GGC	GAG	GAG	CTG	TTC	ACC	GGG	GTG	GTG	CCC	ATC	CTG	GTC	GAG	2880
	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	Val	Glu	
		945				950				955					960		
35	CTG	GAC	GGC	GAC	GTA	AAC	GGC	CAC	AAG	TTC	AGC	GTG	TCC	GGC	GAG	GGC	2928
	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	Glu	Gly	
				965				970						975			
	GAG	GGC	GAT	GCC	ACC	TAC	GGC	AAG	CTG	ACC	CTG	AAG	TTC	ATC	TGC	ACC	2976
	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	Cys	Thr	
				980				985					990				
40	ACC	GGC	AAG	CTG	CCC	GTG	CCC	TGG	CCC	ACC	CTC	GTG	ACC	ACC	CTG	ACC	3024
	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	Leu	Thr	
			995				1000					1005					
45	TAC	GGC	GTG	CAG	TGC	TTC	AGC	CGC	TAC	CCC	GAC	CAC	ATG	AAG	CAG	CAC	3072
	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	Gln	His	
		1010					1015				1020						
	GAG	TTC	TTC	AAG	TCC	GCC	AGC	GGC	GAT	CCA	CCG	GTC	GCC	ACC	ATG	GTG	
55	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	Val	Lys	3120
				1045						1050				1055			
	TTC	GAT	GGC	CAG	AGC	TTT	ATG	AAA	CTT	ATG	GGT	TCC	TAC	CCC	ACA	GTC	

266

Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
 1060 1065 1070

5 TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC TAC 3264
 Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr
 1075 1080 1085

10 AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC ATC 3312
 Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile
 1090 1095 1100

15 AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG 3360
 Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln
 1105 1110 1115 1120

CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG 3408
 Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
 1125 1130 1135

20 CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA 3456
 Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
 1140 1145 1150

25 GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC 3504
 Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr
 1155 1160 1165

30 GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA 3546
 Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
 1170 1175 1180

(2) INFORMATION FOR SEQ ID NO:133:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1181 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: protein
 (v) FRAGMENT TYPE: internal

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:

Met Asn Ala Pro Glu Arg Gln Pro Gln Pro Asp Gly Gly Asp Ala Pro
 1 5 10 15
 Gly His Glu Pro Gly Gly Ser Pro Gln Asp Gly Leu Ser Phe Ser
 20 25 30 35 40 45 50 55 60
 Met Asp Tyr Gly Leu Lys Pro Tyr Ser Pro Leu Ala Ser Leu Ser Gly
 55 60 65 70 75 80
 Glu Pro Pro Gly Asp Phe Glu Glu Ser Asp Val Glu Ser Glu Ser

267

				85				90					95			
	Phe	Leu	Ser	Ala	Ala	Lys	Pro	Ala	Gly	Ala	Ser	Gly	Leu	Ser	Pro	Arg
				100					105					110		
5	Ile	Glu	Ile	Thr	Pro	Ser	His	Glu	Leu	Ile	Gln	Ala	Val	Gly	Pro	Leu
			115					120					125			
	Arg	Met	Arg	Asp	Ala	Gly	Leu	Leu	Val	Glu	Gln	Pro	Pro	Leu	Ala	Gly
		130				135						140				
	Val	Ala	Ala	Ser	Pro	Arg	Phe	Thr	Leu	Pro	Val	Pro	Gly	Phe	Glu	Gly
	145					150					155				160	
10	Tyr	Arg	Glu	Pro	Leu	Cys	Leu	Ser	Pro	Ala	Ser	Ser	Gly	Ser	Ser	Ala
				165					170					175		
	Ser	Phe	Ile	Ser	Asp	Thr	Phe	Ser	Pro	Tyr	Thr	Ser	Pro	Cys	Val	Ser
			180					185					190			
	Pro	Asn	Asn	Gly	Gly	Pro	Asp	Asp	Leu	Cys	Pro	Gln	Phe	Gln	Asn	Ile
15			195				200					205				
	Pro	Ala	His	Tyr	Ser	Pro	Arg	Thr	Ser	Pro	Ile	Met	Ser	Pro	Arg	Thr
	210					215					220					
	Ser	Leu	Ala	Glu	Asp	Ser	Cys	Leu	Gly	Arg	His	Ser	Pro	Val	Pro	Arg
	225					230					235				240	
20	Pro	Ala	Ser	Arg	Ser	Ser	Ser	Pro	Gly	Ala	Lys	Arg	Arg	His	Ser	Cys
				245					250					255		
	Ala	Glu	Ala	Leu	Val	Ala	Leu	Pro	Pro	Gly	Ala	Ser	Pro	Gln	Arg	Ser
			260					265					270			
25	Arg	Ser	Pro	Ser	Pro	Gln	Pro	Ser	Ser	His	Val	Ala	Pro	Gln	Asp	His
		275					280					285				
	Gly	Ser	Pro	Ala	Gly	Tyr	Pro	Pro	Val	Ala	Gly	Ser	Ala	Val	Ile	Met
	290					295					300					
	Asp	Ala	Leu	Asn	Ser	Leu	Ala	Thr	Asp	Ser	Pro	Cys	Gly	Ile	Pro	Pro
	305				310					315				320		
30	Lys	Met	Trp	Lys	Thr	Ser	Pro	Asp	Pro	Ser	Pro	Val	Ser	Ala	Ala	Pro
				325					330					335		
	Ser	Lys	Ala	Gly	Leu	Pro	Arg	His	Ile	Tyr	Pro	Ala	Val	Glu	Phe	Leu
			340					345					350			
	Gly	Pro	Cys	Glu	Gln	Gly	Glu	Arg	Arg	Asn	Ser	Ala	Pro	Glu	Ser	Ile
35			355				360					365				
	Leu	Leu	Val	Pro	Pro	Thr	Trp	Pro	Lys	Pro	Leu	Val	Pro	Ala	Ile	Pro
	370					375					380					
	Ile	Cys	Ser	Ile	Pro	Val	Thr	Ala	Ser	Leu	Pro	Pro	Leu	Glu	Trp	Pro
	385				390					395				400		
40	Leu	Ser	Ser	Gln	Ser	Gly	Ser	Tyr	Glu	Leu	Arg	Ile	Glu	Val	Gln	Pro
				405					410				415			
	Lys	Pro	His	His	Arg	Ala	His	Tyr	Glu	Thr	Glu	Gly	Ser	Arg	Gly	Ala
			420					425					430			
45	Val	Lys	Ala	Pro	Thr	Gly	Gly	His	Pro	Val	Val	Gln	Leu	His	Gly	Tyr
		435					440					445				
	Met	Glu	Asn	Lys	Pro	Leu	Gly	Leu	Gln	Ile	Phe	Ile	Gly	Thr	Ala	Asp
	450					455					460					
	Glu	Arg	Ile	Leu	Lys	Pro	His	Ala	Phe	Thr	Gly	Val	Val	Val	Val	Val
				500				505					510			
55	Ile	Asp	Cys	Ala	Gly	Ile	Leu	Lys	Leu	Arg	Asn	Ala	Asp	Ile	Glu	Leu
		515					520					525				
	Arg	Lys	Gly	Glu	Thr	Ser	Ala	Gly	Thr	Ser	Thr	Arg	Thr	Arg	Thr	Arg

[illegible]

				980					985					990						
		Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	Leu	Thr			
				995					1000					1005						
5		Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	Gln	His			
		1010						1015					1020							
		Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	Arg	Thr			
		025				1030						1035				1040				
		Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	Val	Lys			
				1045						1050					1055					
10		Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	Ile	Asp			
		1060							1065					1070						
		Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	Asn	Tyr			
		1075				1080						1085								
		Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	Gly	Ile			
15		1090				1095						1100								
		Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	Val	Gln			
		105			1110						1115				1120					
		Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	Pro	Val			
				1125						1130					1135					
20		Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	Ser	Lys			
		1140				1145						1150								
		Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	Val	Thr			
		1155				1160						1165								
		Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys						
25		1170				1175						1180								

30 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2802 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

40 (A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2799
(D) OTHER INFORMATION:

ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu

1 5 10 15

GTC GAG GTG GAC GGC GCG GTA TTA GGA AAA AAT ATT ...

144
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
 35 40 45

55

270

	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	
	50						55					60					
5	CTG	ACC	TAC	GGC	GTG	CAG	TGC	TTC	AGC	CGC	TAC	CCC	GAC	CAC	ATG	AAG	240
	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	
	65					70					75					80	
10	CAG	CAC	GAC	TTC	TTC	AAG	TCC	GCC	ATG	CCC	GAA	GGC	TAC	GTC	CAG	GAG	288
	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	
					85					90					95		
15	CGC	ACC	ATC	TTC	TTC	AAG	GAC	GAC	GGC	AAC	TAC	AAG	ACC	CGC	GCC	GAG	336
	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Cly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	
				100					105					110			
	GTG	AAG	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	CGC	ATC	GAG	CTG	AAG	GGC	384
	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	
			115					120					125				
20	ATC	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	CAC	AAG	CTG	GAG	TAC	432
	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	
		130					135					140					
25	AAC	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	GAC	AAG	CAG	AAG	AAC	480
	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	
	145					150					155					160	
30	GGC	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	ATC	GAG	GAC	GGC	AGC	528
	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	
					165				170						175		
35	GTG	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	CCC	ATC	GGC	GAC	GGC	576
	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	
				180					185					190			
	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	ACC	CAG	TCC	GCC	CTG	624
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	
			195					200					205				
40	AGC	AAA	GAC	CCC	AAC	GAG	AAG	CGC	GAT	CAC	ATG	GTC	CTG	CTG	GAG	TTC	672
	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	
		210					215					220					
45	GTG	ACC	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	GAG	CTG	TAC	AAG	TCC	720
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser	
	225					230					235					240	
55	GGG	CTC	AGA	TCT	GGA	GCG	ATG	ATG	GGG	ATG	ATG	ATG	ATG	ATG	ATG	ATG	
	Ala	Leu	Gln	Glu	Lys	Ile	Glu	Glu	Leu	Arg	Gln	Arg	Asp	Ala	Leu	Ile	
				260					265					270			

271

[illegible]

272

	Asp	Val	Leu	Glu	Glu	Thr	His	Tyr	Glu	Asn	Gly	Glu	Tyr	Ile	Ile	Arg	
				500					505					510			
5	CAA	GGT	GCA	AGA	GGG	GAC	ACC	TTC	TTT	ATC	ATC	AGC	AAA	GGA	ACG	GTA	1584
	Gln	Gly	Ala	Arg	Gly	Asp	Thr	Phe	Phe	Ile	Ile	Ser	Lys	Gly	Thr	Val	
			515					520					525				
10	AAT	GTC	ACT	CGT	GAA	GAC	TCA	CCG	AGT	GAA	GAC	CCA	GTC	TTT	CTT	AGA	1632
	Asn	Val	Thr	Arg	Glu	Asp	Ser	Pro	Ser	Glu	Asp	Pro	Val	Phe	Leu	Arg	
		530					535					540					
15	ACT	TTA	GGA	AAA	GGA	GAC	TGG	TTT	GGA	GAG	AAA	GCC	TTG	CAG	GGG	GAA	1680
	Thr	Leu	Gly	Lys	Gly	Asp	Trp	Phe	Gly	Glu	Lys	Ala	Leu	Gln	Gly	Glu	
	545					550					555					560	
	GAT	GTG	AGA	ACA	GCA	AAC	GTA	ATT	GCT	GCA	GAA	GCT	GTA	ACC	TGC	CTT	1728
	Asp	Val	Arg	Thr	Ala	Asn	Val	Ile	Ala	Ala	Glu	Ala	Val	Thr	Cys	Leu	
					565				570						575		
20	GTG	ATT	GAC	AGA	GAC	TCT	TTT	AAA	CAT	TTG	ATT	GGA	GGG	CTG	GAT	GAT	1776
	Val	Ile	Asp	Arg	Asp	Ser	Phe	Lys	His	Leu	Ile	Gly	Gly	Leu	Asp	Asp	
				580					585					590			
25	GTT	TCT	AAT	AAA	GCA	TAT	GAA	GAT	GCA	GAA	GCT	AAA	GCA	AAA	TAT	GAA	1824
	Val	Ser	Asn	Lys	Ala	Tyr	Glu	Asp	Ala	Glu	Ala	Lys	Ala	Lys	Tyr	Glu	
			595					600					605				
30	GCT	GAA	GCG	GCT	TTC	TTC	GCC	AAC	CTG	AAG	CTG	TCT	GAT	TTC	AAC	ATC	1872
	Ala	Glu	Ala	Ala	Phe	Phe	Ala	Asn	Leu	Lys	Leu	Ser	Asp	Phe	Asn	Ile	
		610					615						620				
35	ATT	GAT	ACC	CTT	GGA	GTT	GGA	GGT	TTC	GGA	CGA	GTA	GAA	CTG	GTC	CAG	1920
	Ile	Asp	Thr	Leu	Gly	Val	Gly	Gly	Phe	Gly	Arg	Val	Glu	Leu	Val	Gln	
	625					630					635					640	
	TTG	AAA	AGT	GAA	GAA	TCC	AAA	ACG	TTT	GCA	ATG	AAG	ATT	CTC	AAG	AAA	1968
	Leu	Lys	Ser	Glu	Glu	Ser	Lys	Thr	Phe	Ala	Met	Lys	Ile	Leu	Lys	Lys	
					645					650					655		
40	CGT	CAC	ATT	GTG	GAC	ACA	AGA	CAG	CAG	GAG	CAC	ATC	CGC	TCA	GAG	AAG	2016
	Arg	His	Ile	Val	Asp	Thr	Arg	Gln	Gln	Glu	His	Ile	Arg	Ser	Glu	Lys	
				660					665					670			
45	CAG	ATC	ATG	CAG	GGG	GCT	CAT	TCC	GAT	TTC	ATA	GTG	AGA	CTG	TAC	AGA	2064
	Gln	Ile	Met	Gln	Gly	Ala	His	Ser	Asp	Phe	Ile	Val	Arg	Leu	Tyr	Arg	
			675					680					685				
	ACA	TTT	AAG	GAC	ACC	AAA	TAT	TTG	TAT	ATG	TTG	ATG	GAA	CTT	CTT	CTT	
55	Gly	Gly	Glu	Leu	Trp	Thr	Ile	Leu	Arg	Asp	Arg	Gly	Ser	Phe	Glu	Asp	
	705					710					715					720	
	TCG	ACA	ACC	ACA	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	TTT	

Ser Thr Thr Arg Phe Tyr Thr Ala Cys Val Val Glu Ala Phe Ala Tyr
725 730 735

10 ATC CTA GAT CAC CGA GGT TAT GCC AAA CTG GTT GAT TTT GGC TTT GCA 2304
Ile Leu Asp His Arg Gly Tyr Ala Lys Leu Val Asp Phe Gly Phe Ala
755 760 765

GAG TAT GTA GCC CCA GAG ATC ATC CTG AAC AAA GGC CAT GAC ATT TCA 2400
Glu Tyr Val Ala Pro Glu Ile Ile Leu Asn Lys Gly His Asp Ile Ser
785 790 795 800

25 AGC CCA CCT TTC TCA GGC CCA GAT CCT ATG AAA ACC TAT AAC ATC ATA 2496
Ser Pro Pro Phe Ser Gly Pro Asp Pro Met Lys Thr Tyr Asn Ile Ile
820 825 830

GCT GCT AAT TTA ATT AAA AAA CTA TGC AGG GAC AAT CCA TCA GAA AGA 2592
Ala Ala Asn Leu Ile Lys Lys Leu Cys Arg Asp Asn Pro Ser Glu Arg
850 855 860

40 TTT GAG GGC TTT AAC TGG GAA GGC TTA AGA AAA GGT ACC TTG ACA CCT 2688
Phe Glu Gly Phe Asn Trp Glu Gly Leu Arg Lys Gly Thr Leu Thr Pro
 885 890 895

AGT TTC CCT GAG GAC AAC GAT GAA CCG CCG CCG GAT GCG GCG GCG GCG

55

274

(2) INFORMATION FOR SEQ ID NO:135:

(i) SEQUENCE CHARACTERISTICS:

5

(A) LENGTH: 933 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

10

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:135:

15 Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1 5 10 15
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
 20 25 30
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
 35 40 45
 20 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 50 55 60
 Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
 65 70 75 80
 Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
 25 85 90 95
 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
 100 105 110
 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
 115 120 125
 30 Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
 130 135 140
 Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
 145 150 155 160
 Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
 35 165 170 175
 Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
 180 185 190
 Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
 195 200 205
 40 Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
 210 215 220
 Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
 225 230 235 240
 Gly Leu Arg Ser Arg Gly Ser Met Gly Thr Leu Arg Asp Leu Gln Tyr
 45 245 250 255
 Ala Leu Gln Glu Lys Ile Glu Glu Leu Arg Gln Arg Asp Ala Leu Ile
 260 265 270

55 Thr Gln Ala Gln Lys Gln Ser Ala Ser Thr Leu Gln Gly Glu Pro Arg
 305 310 315 320
 Thr Lys Arg Gln Ala Ile Ser Ala Glu Pro Thr Ala Phe Asp Ile Gln
 325 330 335

[illegible]

276

785 790 795 800
 Ala Asp Tyr Trp Ser Leu Gly Ile Leu Met Tyr Glu Leu Leu Thr Gly
 805 810 815
 5 Ser Pro Pro Phe Ser Gly Pro Asp Pro Met Lys Thr Tyr Asn Ile Ile
 820 825 830
 Leu Arg Gly Ile Asp Met Ile Glu Phe Pro Lys Lys Ile Ala Lys Asn
 835 840 845
 Ala Ala Asn Leu Ile Lys Lys Leu Cys Arg Asp Asn Pro Ser Glu Arg
 850 855 860
 10 Leu Gly Asn Leu Lys Asn Gly Val Lys Asp Ile Gln Lys His Lys Trp
 865 870 875 880
 Phe Glu Gly Phe Asn Trp Glu Gly Leu Arg Lys Gly Thr Leu Thr Pro
 885 890 895
 15 Pro Ile Ile Pro Ser Val Ala Ser Pro Thr Asp Thr Ser Asn Phe Asp
 900 905 910
 Ser Phe Pro Glu Asp Asn Asp Glu Pro Pro Pro Asp Asp Asn Ser Gly
 915 920 925
 Trp Asp Ile Asp Phe
 930

20

(2) INFORMATION FOR SEQ ID NO:136:

(i) SEQUENCE CHARACTERISTICS:

- 25 (A) LENGTH: 2799 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

30

(ix) FEATURE:

- (A) NAME/KEY: Coding Sequence
 (B) LOCATION: 1...2795
 (D) OTHER INFORMATION:

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:136:

40 ATG GGC ACC TTG CGG GAT TTA CAG TAC GCG CTC CAG GAG AAG ATC GAG 48
 Met Gly Thr Leu Arg Asp Leu Gln Tyr Ala Leu Gln Glu Lys Ile Glu
 1 5 10 15
 GAG CTG AGG CAG CGG GAT GCT CTC ATC GAC GAG CTG GAG CTG GAG TTG 96
 Glu Leu Arg Gln Arg Asp Ala Leu Ile Asp Glu Leu Glu Leu Glu Leu
 20 25 30
 45 GAT CAG AAG GAC GAA CTG ATC CAG AAG CTG CAG AAC GAG CTG GAC AAG 144
 Asp Gln Lys Asp Glu Leu Ile Gln Lys Leu Gln Asn Glu Leu Asp Lys
 35 40 45
 55 GCG AGC ACC TTG CAG GGC GAG CCG CGC ACC AAG CGG CAG GCG ATC TCC 240
 Ala Ser Thr Leu Gln Gly Glu Pro Arg Thr Lys Arg Gln Ala Ile Ser
 55 60 65

277

5	GCC	GAG	CCC	ACC	GCC	TTC	GAC	ATC	CAG	GAT	CTC	AGC	CAT	GTG	ACC	CTG	288
	Ala	Glu	Pro	Thr	Ala	Phe	Asp	Ile	Gln	Asp	Leu	Ser	His	Val	Thr	Leu	
	85				90				95								
10	CCC	TTC	TAC	CCC	AAG	AGC	CCA	CAG	TCC	AAG	GAT	CTT	ATA	AAG	GAA	GCT	336
	Pro	Phe	Tyr	Pro	Lys	Ser	Pro	Gln	Ser	Lys	Asp	Leu	Ile	Lys	Glu	Ala	
	100				105				110								
15	ATC	CTT	GAC	AAT	GAC	TTT	ATG	AAG	AAC	TTG	GAG	CTG	TCG	CAG	ATC	CAG	384
	Ile	Leu	Asp	Asn	Asp	Phe	Met	Lys	Asn	Leu	Glu	Leu	Ser	Gln	Ile	Gln	
	115				120				125								
20	GAG	ATT	GTG	GAT	TGT	ATG	TAC	CCG	GTG	GAG	TAT	GGC	AAG	GAC	AGT	TGC	432
	Glu	Ile	Val	Asp	Cys	Met	Tyr	Pro	Val	Glu	Tyr	Gly	Lys	Asp	Ser	Cys	
	130				135				140								
25	ATC	ATC	AAA	GAA	GGA	GAC	GTG	GGG	TCA	CTG	GTG	TAT	GTC	ATG	GAA	GAT	480
	Ile	Ile	Lys	Glu	Gly	Asp	Val	Gly	Ser	Leu	Val	Tyr	Val	Met	Glu	Asp	
	145				150				155								
30	GGT	AAG	GTT	GAA	GTT	ACA	AAA	GAA	GGT	GTG	AAG	TTG	TGT	ACC	ATG	GGT	528
	Gly	Lys	Val	Glu	Val	Thr	Lys	Glu	Gly	Val	Lys	Leu	Cys	Thr	Met	Gly	
	165				170				175								
35	CCA	GGA	AAA	GTG	TTT	GGG	GAA	TTG	GCT	ATT	CTT	TAC	AAC	TGT	ACC	CGG	576
	Pro	Gly	Lys	Val	Phe	Gly	Glu	Leu	Ala	Ile	Leu	Tyr	Asn	Cys	Thr	Arg	
	180				185				190								
40	ACA	GCG	ACC	GTC	AAG	ACT	CTT	GTA	AAT	GTA	AAA	CTC	TGG	GCC	ATT	GAT	624
	Thr	Ala	Thr	Val	Lys	Thr	Leu	Val	Asn	Val	Lys	Leu	Trp	Ala	Ile	Asp	
	195				200				205								
45	CGA	CAA	TGT	TTT	CAA	ACA	ATA	ATG	ATG	AGG	ACA	GGA	CTC	ATC	AAG	CAT	672
	Arg	Gln	Cys	Phe	Gln	Thr	Ile	Met	Met	Arg	Thr	Gly	Leu	Ile	Lys	His	
	210				215				220								
50	ACC	GAG	TAT	ATG	GAA	TTT	TTA	AAA	AGC	GTT	CCA	ACA	TTC	CAG	AGC	CTT	720
	Thr	Glu	Tyr	Met	Glu	Phe	Leu	Lys	Ser	Val	Pro	Thr	Phe	Gln	Ser	Leu	
	225				230				235								
55	CCT	GAA	GAG	ATC	CTC	AGC	AAG	CTT	GCT	GAT	GTC	CTT	GAA	GAG	ACC	CAC	768
	Pro	Glu	Glu	Ile	Leu	Ser	Lys	Leu	Ala	Asp	Val	Leu	Glu	Glu	Thr	His	
	245				250				255								
60	TAT	GAA	AAT	GGA	GAA	TAT	ATT	ATC	AGG	CAA	GGT	GCA	AGA	GGG	GAC	ACC	816
	Tyr	Glu	Asn	Gly	Glu	Tyr	Ile	Ile	Arg	Gln	Gly	Ala	Arg	Gly	Asp	Thr	
	260				265				270								
65	CCG	AGT	GAA	GAC	CCA	GTC	TTT	CTT	AGA	ACT	TTA	GGA	AAA	GGA	GAC	TGG	912
	Pro	Ser	Glu	Asp	Pro	Val	Phe	Leu	Arg	Thr	Leu	Gly	Lys	Gly	Asp	Trp	
	275				280				285								

278

5	TTT GGA GAG AAA GCC TTG CAG GGG GAA GAT GTG AGA ACA GCA AAC GTA	960
	Phe Gly Glu Lys Ala Leu Gln Gly Glu Asp Val Arg Thr Ala Asn Val	
	305 310 315 320	
10	ATT GCT GCA GAA GCT GTA ACC TGC CTT GTG ATT GAC AGA GAC TCT TTT	1008
	Ile Ala Ala Glu Ala Val Thr Cys Leu Val Ile Asp Arg Asp Ser Phe	
	325 330 335	
15	AAA CAT TTG ATT GGA GGG CTG GAT GAT GTT TCT AAT AAA GCA TAT GAA	1056
	Lys His Leu Ile Gly Gly Leu Asp Asp Val Ser Asn Lys Ala Tyr Glu	
	340 345 350	
20	GAT GCA GAA GCT AAA GCA AAA TAT GAA GCT GAA GCG GCT TTC TTC GCC	1104
	Asp Ala Glu Ala Lys Ala Lys Tyr Glu Ala Glu Ala Ala Phe Phe Ala	
	355 360 365	
25	AAC CTG AAG CTG TCT GAT TTC AAC ATC ATT GAT ACC CTT GGA GTT GGA	1152
	Asn Leu Lys Leu Ser Asp Phe Asn Ile Ile Asp Thr Leu Gly Val Gly	
	370 375 380	
30	GGT TTC GGA CGA GTA GAA CTG GTC CAG TTG AAA AGT GAA GAA TCC AAA	1200
	Gly Phe Gly Arg Val Glu Leu Val Gln Leu Lys Ser Glu Glu Ser Lys	
	385 390 395 400	
35	ACG TTT GCA ATG AAG ATT CTC AAG AAA CGT CAC ATT GTG GAC ACA AGA	1248
	Thr Phe Ala Met Lys Ile Leu Lys Lys Arg His Ile Val Asp Thr Arg	
	405 410 415	
40	CAG CAG GAG CAC ATC CGC TCA GAG AAG CAG ATC ATG CAG GGG GCT CAT	1296
	Gln Gln Glu His Ile Arg Ser Glu Lys Gln Ile Met Gln Gly Ala His	
	420 425 430	
45	TCC GAT TTC ATA GTG AGA CTG TAC AGA ACA TTT AAG GAC AGC AAA TAT	1344
	Ser Asp Phe Ile Val Arg Leu Tyr Arg Thr Phe Lys Asp Ser Lys Tyr	
	435 440 445	
50	TTG TAT ATG TTG ATG GAA GCT TGT CTA GGT GGA GAG CTC TGG ACC ATT	1392
	Leu Tyr Met Leu Met Glu Ala Cys Leu Gly Gly Glu Leu Trp Thr Ile	
	450 455 460	
55	CTC AGG GAT AGA GGT TCG TTT GAA GAT TCT ACA ACC AGA TTT TAC ACA	1440
	Leu Arg Asp Arg Gly Ser Phe Glu Asp Ser Thr Thr Arg Phe Tyr Thr	
	465 470 475 480	
60	GCA TGT GTG GTA GAA GCT TTT GCC TAT CTG CAT TCC AAA GGA ATC ATT	1488
	Ala Cys Val Val Glu Ala Phe Ala Tyr Leu His Ser Lys Gly Ile Ile	
	485 490 495	
65	GCC AAA CTG GTT GAT TTT GGC TTT GCA AAG AAA ATA GGA TTT GGA AAG	1584
	Ala Lys Leu Val Asp Phe Gly Phe Ala Lys Lys Ile Gly Phe Gly Lys	
	500 505 510	

279

5	AAA ACA TGG ACT TTT TGT GGG ACT CCA GAG TAT GTA GCC CCA GAG ATC	1632
	Lys Thr Trp Thr Phe Cys Gly Thr Pro Glu Tyr Val Ala Pro Glu Ile	
	530 535 540	
10	ATC CTG AAC AAA GGC CAT GAC ATT TCA GCC GAC TAC TGG TCA CTG GGA	1680
	Ile Leu Asn Lys Gly His Asp Ile Ser Ala Asp Tyr Trp Ser Leu Gly	
	545 550 555 560	
15	ATC CTA ATG TAT GAA CTC CTG ACT GGC AGC CCA CCT TTC TCA GGC CCA	1728
	Ile Leu Met Tyr Glu Leu Leu Thr Gly Ser Pro Pro Phe Ser Gly Pro	
	565 570 575	
20	GAT CCT ATG AAA ACC TAT AAC ATC ATA TTG AGG GGG ATT GAC ATG ATA	1776
	Asp Pro Met Lys Thr Tyr Asn Ile Ile Leu Arg Gly Ile Asp Met Ile	
	580 585 590	
25	GAA TTT CCA AAG AAG ATT GCC AAA AAT GCT GCT AAT TTA ATT AAA AAA	1824
	Glu Phe Pro Lys Lys Ile Ala Lys Asn Ala Ala Asn Leu Ile Lys Lys	
	595 600 605	
30	CTA TGC AGG GAC AAT CCA TCA GAA AGA TTA GGG AAT TTG AAA AAT GGA	1872
	Leu Cys Arg Asp Asn Pro Ser Glu Arg Leu Gly Asn Leu Lys Asn Gly	
	610 615 620	
35	GTA AAA GAC ATT CAA AAG CAC AAA TGG TTT GAG GGC TTT AAC TGG GAA	1920
	Val Lys Asp Ile Gln Lys His Lys Trp Phe Glu Gly Phe Asn Trp Glu	
	625 630 635 640	
40	GGC TTA AGA AAA GGT ACC TTG ACA CCT CCT ATA ATA CCA AGT GTT GCA	1968
	Gly Leu Arg Lys Gly Thr Leu Thr Pro Pro Ile Ile Pro Ser Val Ala	
	645 650 655	
45	TCA CCC ACA GAC ACA AGT AAT TTT GAC AGT TTC CCT GAG GAC AAC GAT	2016
	Ser Pro Thr Asp Thr Ser Asn Phe Asp Ser Phe Pro Glu Asp Asn Asp	
	660 665 670	
50	GAA CCA CCA CCT GAT GAC AAC TCA GGA TGG GAT ATA GAC TTC TCG GAT	2064
	Glu Pro Pro Pro Asp Asp Asn Ser Gly Trp Asp Ile Asp Phe Ser Asp	
	675 680 685	
55	CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG	2112
	Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly	
	690 695 700	
60	GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG	2160
	Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys	
	705 710 715 720	
65	ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC	2256
	Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro	
	725 730 735 740	

280

5	ACC	CTC	GTG	ACC	ACC	CTG	ACC	TAC	GGC	GTG	CAG	TGC	TTC	AGC	CGC	TAC	2304
	Thr	Leu	Val	Thr	Thr	Leu	Thr	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	
	755			760			765										
10	CCC	GAC	CAC	ATG	AAG	CAG	CAC	GAC	TTC	TTC	AAG	TCC	GCC	ATG	CCC	GAA	2352
	Pro	Asp	His	Met	Lys	Gln	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	
	770			775			780										
15	GGC	TAC	GTC	CAG	GAG	CGC	ACC	ATC	TTC	TTC	AAG	GAC	GAC	GGC	AAC	TAC	2400
	Gly	Tyr	Val	Gln	Glu	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	
	785			790			795			800							
20	AAG	ACC	CGC	GCC	GAG	GTG	AAG	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	CGC	2448
	Lys	Thr	Arg	Ala	Glu	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	
	805			810			815										
25	ATC	GAG	CTG	AAG	GGC	ATC	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	2496
	Ile	Glu	Leu	Lys	Gly	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	
	820			825			830										
30	CAC	AAG	CTG	GAG	TAC	AAC	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	2544
	His	Lys	Leu	Glu	Tyr	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	
	835			840			845										
35	GAC	AAG	CAG	AAG	AAC	GGC	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	2592
	Asp	Lys	Gln	Lys	Asn	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	
	850			855			860										
40	ATC	GAG	GAC	GGC	AGC	GTG	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	2640
	Ile	Glu	Asp	Gly	Ser	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	
	865			870			875			880							
45	CCC	ATC	GGC	GAC	GGC	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	2688
	Pro	Ile	Gly	Asp	Gly	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	
	885			890			895										
50	ACC	CAG	TCC	GCC	CTG	AGC	AAA	GAC	CCC	AAC	GAG	AAG	CGC	GAT	CAC	ATG	2736
	Thr	Gln	Ser	Ala	Leu	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	
	900			905			910										
55	GTC	CTG	CTG	GAG	TTC	GTG	ACC	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	2784
	Val	Leu	Leu	Glu	Phe	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	
	915			920			925										
60	GAG	CTG	TAC	AA	GTAA												2799
	Glu	Leu	Tyr	Lys													

(1) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 932 amino acids

(B) TYPE: amino acid

(C) TRANSLATION: (1000)

281

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:

Met Gly Thr Leu Arg Asp Leu Gln Tyr Ala Leu Gln Glu Lys Ile Glu
 1 5 10 15
 10 Glu Leu Arg Gln Arg Asp Ala Leu Ile Asp Glu Leu Glu Leu Glu Leu
 20 25 30
 Asp Gln Lys Asp Glu Leu Ile Gln Lys Leu Gln Asn Glu Leu Asp Lys
 35 40 45
 15 Tyr Arg Ser Val Ile Arg Pro Ala Thr Gln Gln Ala Gln Lys Gln Ser
 50 55 60
 Ala Ser Thr Leu Gln Gly Glu Pro Arg Thr Lys Arg Gln Ala Ile Ser
 65 70 75 80
 Ala Glu Pro Thr Ala Phe Asp Ile Gln Asp Leu Ser His Val Thr Leu
 85 90 95
 20 Pro Phe Tyr Pro Lys Ser Pro Gln Ser Lys Asp Leu Ile Lys Glu Ala
 100 105 110
 Ile Leu Asp Asn Asp Phe Met Lys Asn Leu Glu Leu Ser Gln Ile Gln
 115 120 125
 25 Glu Ile Val Asp Cys Met Tyr Pro Val Glu Tyr Gly Lys Asp Ser Cys
 130 135 140
 Ile Ile Lys Glu Gly Asp Val Gly Ser Leu Val Tyr Val Met Glu Asp
 145 150 155 160
 Gly Lys Val Glu Val Thr Lys Glu Gly Val Lys Leu Cys Thr Met Gly
 165 170 175
 30 Pro Gly Lys Val Phe Gly Glu Leu Ala Ile Leu Tyr Asn Cys Thr Arg
 180 185 190
 Thr Ala Thr Val Lys Thr Leu Val Asn Val Lys Leu Trp Ala Ile Asp
 195 200 205
 35 Arg Gln Cys Phe Gln Thr Ile Met Met Arg Thr Gly Leu Ile Lys His
 210 215 220
 Thr Glu Tyr Met Glu Phe Leu Lys Ser Val Pro Thr Phe Gln Ser Leu
 225 230 235 240
 Pro Glu Glu Ile Leu Ser Lys Leu Ala Asp Val Leu Glu Glu Thr His
 245 250 255
 40 Tyr Glu Asn Gly Glu Tyr Ile Ile Arg Gln Gly Ala Arg Gly Asp Thr
 260 265 270
 Phe Phe Ile Ile Ser Lys Gly Thr Val Asn Val Thr Arg Glu Asp Ser
 275 280 285
 45 Pro Ser Glu Asp Pro Val Phe Leu Arg Thr Leu Gly Lys Gly Asp Trp
 290 295 300
 Phe Gly Glu Lys Ala Leu Gln Gly Glu Asp Val Arg Thr Ala Asn Val
 305 310 315 320
 Ile Ala Ala Glu Ala Val Thr Cys Leu Val Ile Asp Thr Thr Thr Thr Thr
 355 360 365
 55 Asn Leu Lys Leu Ser Asp Phe Asn Ile Ile Asp Thr Leu Gly Val Gly
 370 375 380
 Gly Phe Gly Arg Val Glu Ile Val Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr

																400
																Arg
																415
																His
5	Gln	Gln	Glu	His	Ile	Arg	Ser	Glu	Lys	Gln	Ile	Met	Gln	Gly	Ala	His
																430
	Ser	Asp	Phe	Ile	Val	Arg	Leu	Tyr	Arg	Thr	Phe	Lys	Asp	Ser	Lys	Tyr
																445
	Leu	Tyr	Met	Leu	Met	Glu	Ala	Cys	Leu	Gly	Gly	Glu	Leu	Trp	Thr	Ile
																460
10	Leu	Arg	Asp	Arg	Gly	Ser	Phe	Glu	Asp	Ser	Thr	Thr	Arg	Phe	Tyr	Thr
																480
	Ala	Cys	Val	Val	Glu	Ala	Phe	Ala	Tyr	Leu	His	Ser	Lys	Gly	Ile	Ile
																495
15	Tyr	Arg	Asp	Leu	Lys	Pro	Glu	Asn	Leu	Ile	Leu	Asp	His	Arg	Gly	Tyr
																510
	Ala	Lys	Leu	Val	Asp	Phe	Gly	Phe	Ala	Lys	Lys	Ile	Gly	Phe	Gly	Lys
																525
	Lys	Thr	Trp	Thr	Phe	Cys	Gly	Thr	Pro	Glu	Tyr	Val	Ala	Pro	Glu	Ile
																540
20	Ile	Leu	Asn	Lys	Gly	His	Asp	Ile	Ser	Ala	Asp	Tyr	Trp	Ser	Leu	Gly
																560
	Ile	Leu	Met	Tyr	Glu	Leu	Leu	Thr	Gly	Ser	Pro	Pro	Phe	Ser	Gly	Pro
																575
25	Asp	Pro	Met	Lys	Thr	Tyr	Asn	Ile	Ile	Leu	Arg	Gly	Ile	Asp	Met	Ile
																590
	Glu	Phe	Pro	Lys	Lys	Ile	Ala	Lys	Asn	Ala	Ala	Asn	Leu	Ile	Lys	Lys
																605
	Leu	Cys	Arg	Asp	Asn	Pro	Ser	Glu	Arg	Leu	Gly	Asn	Leu	Lys	Asn	Gly
																620
30	Val	Lys	Asp	Ile	Gln	Lys	His	Lys	Trp	Phe	Glu	Gly	Phe	Asn	Trp	Glu
																640
	Gly	Leu	Arg	Lys	Gly	Thr	Leu	Thr	Pro	Pro	Ile	Ile	Pro	Ser	Val	Ala
																655
35	Ser	Pro	Thr	Asp	Thr	Ser	Asn	Phe	Asp	Ser	Phe	Pro	Glu	Asp	Asn	Asp
																670
	Glu	Pro	Pro	Asp	Asp	Asn	Ser	Gly	Trp	Asp	Ile	Asp	Phe	Ser	Asp	
																685
	Pro	Pro	Val	Ala	Thr	Met	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly
																700
40	Val	Val	Pro	Ile	Leu	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys
																720
	Phe	Ser	Val	Ser	Gly	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu
																735
45	Thr	Leu	Lys	Phe	I											

[illegible]

(D) OTHER INFORMATION:

79 Val Ser His Thr Thr Asn Thr Ser Arg Ser Gln Ser Thr Tyr Val Gln Gln
 Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
 85 90 95

284

	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	
				100					105					110			
5	GTG	AAG	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	CGC	ATC	GAG	CTG	AAG	GGC	384
	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	
			115					120					125				
10	ATC	GAC	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	CAC	AAG	CTG	GAG	TAC	432
	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	
		130					135					140					
15	AAC	TAC	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	GAC	AAG	CAG	AAG	AAC	480
	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	
	145					150					155					160	
	GGC	ATC	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	ATC	GAG	GAC	GGC	AGC	528
	Gly	Ile	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	
					165				170						175		
20	GTG	CAG	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	CCC	ATC	GGC	GAC	GGC	576
	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	
				180					185					190			
25	CCC	GTG	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	ACC	CAG	TCC	GCC	CTG	624
	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	
			195					200					205				
30	AGC	AAA	GAC	CCC	AAC	GAG	AAG	CGC	GAT	CAC	ATG	GTC	CTG	CTG	GAG	TTC	672
	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	
		210					215					220					
35	GTG	ACC	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	GAG	CTG	TAC	AAG	TCC	720
	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser	
	225					230					235					240	
	GGA	CTC	AGA	TCT	CGA	GGC	ACC	ATG	AGC	GAC	GTG	GCT	ATT	GTG	AAG	GAG	768
	Gly	Leu	Arg	Ser	Arg	Gly	Thr	Met	Ser	Asp	Val	Ala	Ile	Val	Lys	Glu	
					245					250					255		
40	GGT	TGG	CTG	CAC	AAA	CGA	GGG	GAG	TAC	ATC	AAG	ACC	TGG	CGG	CCA	CGC	816
	Gly	Trp	Leu	His	Lys	Arg	Gly	Glu	Tyr	Ile	Lys	Thr	Trp	Arg	Pro	Arg	
				260					265					270			
45	TAC	TTC	CTC	CTC	AAG	AAT	GAT	GGC	ACC	TTC	ATT	GGC	TAC	AAG	GAG	CGG	864
	Tyr	Phe	Leu	Leu	Lys	Asn	Asp	Gly	Thr	Phe	Ile	Gly	Tyr	Lys	Glu	Arg	
			275					280					285				
55	960
	Ala	Gln	Cys	Gln	Leu	Met	Lys	Thr	Glu	Arg	Pro	Arg	Pro	Asn	Thr	Phe	
	305					310					315					320	

285

	Ile	Ile	Arg	Cys	Leu	Gln	Trp	Thr	Thr	Val	Ile	Glu	Arg	Thr	Phe	His	
					325					330					335		
5	GTG	GAG	ACT	CCT	GAG	GAG	CGG	GAG	GAG	TGG	ACA	ACC	GCC	ATC	CAG	ACT	1056
	Val	Glu	Thr	Pro	Glu	Glu	Arg	Glu	Glu	Trp	Thr	Thr	Ala	Ile	Gln	Thr	
				340				345					350				
10	GTG	GCT	GAC	GGC	CTC	AAG	AAG	CAG	GAG	GAG	GAG	GAG	ATG	GAC	TTC	CGG	1104
	Val	Ala	Asp	Gly	Leu	Lys	Lys	Gln	Glu	Glu	Glu	Glu	Met	Asp	Phe	Arg	
			355					360					365				
15	TCG	GGC	TCA	CCC	AGT	GAC	AAC	TCA	GGG	GCT	GAA	GAG	ATG	GAG	GTG	TCC	1152
	Ser	Gly	Ser	Pro	Ser	Asp	Asn	Ser	Gly	Ala	Glu	Glu	Met	Glu	Val	Ser	
		370					375				380						
20	CTG	GCC	AAG	CCC	AAG	CAC	CGC	GTG	ACC	ATG	AAC	GAG	TTT	GAG	TAC	CTG	1200
	Leu	Ala	Lys	Pro	Lys	His	Arg	Val	Thr	Met	Asn	Glu	Phe	Glu	Tyr	Leu	
	385					390					395					400	
25	AAG	CTG	CTG	GGC	AAG	GGC	ACT	TTC	GGC	AAG	GTG	ATC	CTG	GTG	AAG	GAG	1248
	Lys	Leu	Leu	Gly	Lys	Gly	Thr	Phe	Gly	Lys	Val	Ile	Leu	Val	Lys	Glu	
				405					410						415		
30	AAG	GCC	ACA	GGC	CGC	TAC	TAC	GCC	ATG	AAG	ATC	CTC	AAG	AAG	GAA	GTC	1296
	Lys	Ala	Thr	Gly	Arg	Tyr	Tyr	Ala	Met	Lys	Ile	Leu	Lys	Lys	Glu	Val	
				420					425					430			
35	ATC	GTG	GCC	AAG	GAC	GAG	GTG	GCC	CAC	ACA	CTC	ACC	GAG	AAC	CGC	GTC	1344
	Ile	Val	Ala	Lys	Asp	Glu	Val	Ala	His	Thr	Leu	Thr	Glu	Asn	Arg	Val	
			435					440					445				
40	CTG	CAG	AAC	TCC	AGG	CAC	CCC	TTC	CTC	ACA	GCC	CTG	AAG	TAC	TCT	TTC	1392
	Leu	Gln	Asn	Ser	Arg	His	Pro	Phe	Leu	Thr	Ala	Leu	Lys	Tyr	Ser	Phe	
		450					455					460					
45	CAG	ACC	CAC	GAC	CGC	CTC	TGC	TTT	GTC	ATG	GAG	TAC	GCC	AAC	GGG	GGC	1440
	Gln	Thr	His	Asp	Arg	Leu	Cys	Phe	Val	Met	Glu	Tyr	Ala	Asn	Gly	Gly	
	465					470					475				480		
50	GAG	CTG	TTC	TTC	CAC	CTG	TCC	CGG	GAA	CGT	GTG	TTC	TCC	GAG	GAC	CGG	1488
	Glu	Leu	Phe	Phe	His	Leu	Ser	Arg	Glu	Arg	Val	Phe	Ser	Glu	Asp	Arg	
					485				490						495		
55	GCC	CGC	TTC	TAT	GGC	GCT	GAG	ATT	GTG	TCA	GCC	CTG	GAC	TAC	CTG	CAC	1536
	Ala	Arg	Phe	Tyr	Gly	Ala	Glu	Ile	Val	Ser	Ala	Leu	Asp	Tyr	Leu	His	
				500					505					510			
60	TTG	GAC	AAG	GAC	GGG	CAC	ATT	AAG	ATC	ACA	GAC	TTC	GGG	CTG	TCC	AAG	1584
	Leu	Asp	Lys	Asp	Gly	His	Ile	Lys	Ile	Thr	Asp	Phe	Gly	Leu	Cys	Lys	
			530					535					540				

286

	Glu	Gly	Ile	Lys	Asp	Gly	Ala	Thr	Met	Lys	Thr	Phe	Cys	Gly	Thr	Pro	
	545					550					555					560	
5	GAG	TAC	CTG	GCC	CCC	GAG	GTG	CTG	GAG	GAC	AAT	GAC	TAC	GGC	CGT	GCA	1728
	Glu	Tyr	Leu	Ala	Pro	Glu	Val	Leu	Glu	Asp	Asn	Asp	Tyr	Gly	Arg	Ala	
				565					570					575			
10	GTG	GAC	TGG	TGG	GGG	CTG	GGC	GTG	GTC	ATG	TAC	GAG	ATG	ATG	TGC	GGT	1776
	Val	Asp	Trp	Trp	Gly	Leu	Gly	Val	Val	Met	Tyr	Glu	Met	Met	Cys	Gly	
				580					585					590			
15	CGC	CTG	CCC	TTC	TAC	AAC	CAG	GAC	CAT	GAG	AAG	CTT	TTT	GAG	CTC	ATC	1824
	Arg	Leu	Pro	Phe	Tyr	Asn	Gln	Asp	His	Glu	Lys	Leu	Phe	Glu	Leu	Ile	
			595					600					605				
	CTC	ATG	GAG	GAG	ATC	CGC	TTC	CCG	CGC	ACG	CTT	GGT	CCC	GAG	GCC	AAG	1872
	Leu	Met	Glu	Glu	Ile	Arg	Phe	Pro	Arg	Thr	Leu	Gly	Pro	Glu	Ala	Lys	
		610					615					620					
20	TCC	TTG	CTT	TCA	GGG	CTG	CTC	AAG	AAG	GAC	CCC	AAG	CAG	AGG	CTT	GGC	1920
	Ser	Leu	Leu	Ser	Gly	Leu	Leu	Lys	Lys	Asp	Pro	Lys	Gln	Arg	Leu	Gly	
		625				630					635					640	
25	GGG	GGC	TCC	GAG	GAC	GCC	AAG	GAG	ATC	ATG	CAG	CAT	CGC	TTC	TTT	GCC	1968
	Gly	Gly	Ser	Glu	Asp	Ala	Lys	Glu	Ile	Met	Gln	His	Arg	Phe	Phe	Ala	
				645						650				655			
30	GGT	ATC	GTG	TGG	CAG	CAC	GTG	TAC	GAG	AAG	AAG	CTC	AGC	CCA	CCC	TTC	2016
	Gly	Ile	Val	Trp	Gln	His	Val	Tyr	Glu	Lys	Lys	Leu	Ser	Pro	Pro	Phe	
				660					665					670			
35	AAG	CCC	CAG	GTC	ACG	TCG	GAG	ACT	GAC	ACC	AGG	TAT	TTT	GAT	GAG	GAG	2064
	Lys	Pro	Gln	Val	Thr	Ser	Glu	Thr	Asp	Thr	Arg	Tyr	Phe	Asp	Glu	Glu	
			675					680					685				
	TTC	ACG	GCC	CAG	ATG	ATC	ACC	ATC	ACA	CCA	CCT	GAC	CAA	GAT	GAC	AGC	2112
	Phe	Thr	Ala	Gln	Met	Ile	Thr	Ile	Thr	Pro	Pro	Asp	Gln	Asp	Asp	Ser	
			690					695				700					
40	ATG	GAG	TGT	GTG	GAC	AGC	GAG	CGC	AGG	CCC	CAC	TTC	CCC	CAG	TTC	TCC	2160
	Met	Glu	Cys	Val	Asp	Ser	Glu	Arg	Arg	Pro	His	Phe	Pro	Gln	Phe	Ser	
		705					710				715					720	
45	TAC	TCG	GCC	AGC	AGC	ACG	GCC	TGA									2184
	Tyr	Ser	Ala	Ser	Ser	Thr	Ala										
						725											

SEQUENCE DATA SUMMARY
 (A) LENGTH: 725 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

55

287

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:139:

5 Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
1 5 10 15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
20 25 30
10 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
35 40 45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
50 55 60
15 Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65 70 75 80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
85 90 95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
100 105 110
20 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
115 120 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
130 135 140
25 Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145 150 155 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
165 170 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
180 185 190
30 Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
195 200 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
210 215 220
35 Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225 230 235 240
Gly Leu Arg Ser Arg Gly Thr Met Ser Asp Val Ala Ile Val Lys Glu
245 250 255
Gly Trp Leu His Lys Arg Gly Glu Tyr Ile Lys Thr Trp Arg Pro Arg
260 265 270
40 Tyr Phe Leu Leu Lys Asn Asp Gly Thr Phe Ile Gly Tyr Lys Glu Arg
275 280 285
Pro Gln Asp Val Asp Gln Arg Glu Ala Pro Leu Asn Asn Phe Ser Val
290 295 300
45 Ala Gln Cys Gln Leu Met Lys Thr Glu Arg Pro Arg Pro Asn Thr Phe
305 310 315 320
Ile Ile Arg Cys Leu Gln Trp Thr Thr Val Ile Glu Arg Thr Phe His
325 330 335

370 375 380
Leu Ala Lys Pro Lys His Arg Val Thr Met Asn Glu Phe Glu Tyr Leu
385 390 395 400

288

				405				410					415			
	Lys	Ala	Thr	Gly	Arg	Tyr	Tyr	Ala	Met	Lys	Ile	Leu	Lys	Lys	Glu	Val
				420				425					430			
5	Ile	Val	Ala	Lys	Asp	Glu	Val	Ala	His	Thr	Leu	Thr	Glu	Asn	Arg	Val
			435					440					445			
	Leu	Gln	Asn	Ser	Arg	His	Pro	Phe	Leu	Thr	Ala	Leu	Lys	Tyr	Ser	Phe
			450				455					460				
	Gln	Thr	His	Asp	Arg	Leu	Cys	Phe	Val	Met	Glu	Tyr	Ala	Asn	Gly	Gly
	465					470				475					480	
10	Glu	Leu	Phe	Phe	His	Leu	Ser	Arg	Glu	Arg	Val	Phe	Ser	Glu	Asp	Arg
				485						490					495	
	Ala	Arg	Phe	Tyr	Gly	Ala	Glu	Ile	Val	Ser	Ala	Leu	Asp	Tyr	Leu	His
			500					505					510			
	Ser	Glu	Lys	Asn	Val	Val	Tyr	Arg	Asp	Leu	Lys	Leu	Glu	Asn	Leu	Met
15			515					520					525			
	Leu	Asp	Lys	Asp	Gly	His	Ile	Lys	Ile	Thr	Asp	Phe	Gly	Leu	Cys	Lys
	530					535					540					
	Glu	Gly	Ile	Lys	Asp	Gly	Ala	Thr	Met	Lys	Thr	Phe	Cys	Gly	Thr	Pro
	545					550				555					560	
20	Glu	Tyr	Leu	Ala	Pro	Glu	Val	Leu	Glu	Asp	Asn	Asp	Tyr	Gly	Arg	Ala
				565						570					575	
	Val	Asp	Trp	Trp	Gly	Leu	Gly	Val	Val	Met	Tyr	Glu	Met	Met	Cys	Gly
			580					585					590			
25	Arg	Leu	Pro	Phe	Tyr	Asn	Gln	Asp	His	Glu	Lys	Leu	Phe	Glu	Leu	Ile
			595					600					605			
	Leu	Met	Glu	Glu	Ile	Arg	Phe	Pro	Arg	Thr	Leu	Gly	Pro	Glu	Ala	Lys
	610					615						620				
	Ser	Leu	Leu	Ser	Gly	Leu	Lys	Lys	Asp	Pro	Lys	Gln	Arg	Leu	Gly	
	625					630				635				640		
30	Gly	Gly	Ser	Glu	Asp	Ala	Lys	Glu	Ile	Met	Gln	His	Arg	Phe	Phe	Ala
				645						650					655	
	Gly	Ile	Val	Trp	Gln	His	Val	Tyr	Glu	Lys	Lys	Leu	Ser	Pro	Pro	Phe
			660					665					670			
	Lys	Pro	Gln	Val	Thr	Ser	Glu	Thr	Asp	Thr	Arg	Tyr	Phe	Asp	Glu	Glu
35			675					680					685			
	Phe	Thr	Ala	Gln	Met	Ile	Thr	Ile	Thr	Pro	Pro	Asp	Gln	Asp	Asp	Ser
	690					695						700				
	Met	Glu	Cys	Val	Asp	Ser	Glu	Arg	Arg	Pro	His	Phe	Pro	Gln	Phe	Ser
	705					710				715					720	
40	Tyr	Ser	Ala	Ser	Ser	Thr	Ala									
				725												

(2) INFORMATION FOR SEQ ID NO:140:

45 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2394 base pairs

(B) TYPE: nucleic acid

SEQUENCE INFORMATION

EX. FEATURE:

55 (A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...2391

(C) OTHER INFORMATION:

289

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:

5	ATG GAC GAA CTG TTC CCC CTC ATC TTC CCG GCA GAG CCA GCC CAG GCC	48
	Met Asp Glu Leu Phe Pro Leu Ile Phe Pro Ala Glu Pro Ala Gln Ala	
	1 5 10 15	
10	TCT GGC CCC TAT GTG GAG ATC ATT GAG CAG CCC AAG CAG CGG GGC ATG	96
	Ser Gly Pro Tyr Val Glu Ile Ile Glu Gln Pro Lys Gln Arg Gly Met	
	20 25 30	
15	CGC TTC CGC TAC AAG TGC GAG GGG CGC TCC GCG GGC AGC ATC CCA GGC	144
	Arg Phe Arg Tyr Lys Cys Glu Gly Arg Ser Ala Gly Ser Ile Pro Gly	
	35 40 45	
20	GAG AGG AGC ACA GAT ACC ACC AAG ACC CAC CCC ACC ATC AAG ATC AAT	192
	Glu Arg Ser Thr Asp Thr Thr Lys Thr His Pro Thr Ile Lys Ile Asn	
	50 55 60	
25	GGC TAC ACA GGA CCA GGG ACA GTG CGC ATC TCC CTG GTC ACC AAG GAC	240
	Gly Tyr Thr Gly Pro Gly Thr Val Arg Ile Ser Leu Val Thr Lys Asp	
	65 70 75 80	
30	CCT CCT CAC CGG CCT CAC CCC CAC GAG CTT GTA GGA AAG GAC TGC CGG	288
	Pro Pro His Arg Pro His Pro His Glu Leu Val Gly Lys Asp Cys Arg	
	85 90 95	
35	GAT GGC TTC TAT GAG GCT GAG CTC TGC CCG GAC CGC TGC ATC CAC AGT	336
	Asp Gly Phe Tyr Glu Ala Glu Leu Cys Pro Asp Arg Cys Ile His Ser	
	100 105 110	
40	TTC CAG AAC CTG GGA ATC CAG TGT GTG AAG AAG CGG GAC CTG GAG CAG	384
	Phe Gln Asn Leu Gly Ile Gln Cys Val Lys Lys Arg Asp Leu Glu Gln	
	115 120 125	
45	GCT ATC AGT CAG CGC ATC CAG ACC AAC AAC AAC CCC TTC CAA GTT CCT	432
	Ala Ile Ser Gln Arg Ile Gln Thr Asn Asn Asn Pro Phe Gln Val Pro	
	130 135 140	
50	ATA GAA GAG CAG CGT GGG GAC TAC GAC CTG AAT GCT GTG CGG CTC TGC	480
	Ile Glu Glu Gln Arg Gly Asp Tyr Asp Leu Asn Ala Val Arg Leu Cys	
	145 150 155 160	
55	TTC CAG GTG ACA GTG CGG GAC CCA TCA GGC AGG CCC CTC CGC CTG CCG	528
	Phe Gln Val Thr Val Arg Asp Pro Ser Gly Arg Pro Leu Arg Leu Pro	
	165 170 175	
60	GAG GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC GGC	576
	Glu Leu Lys Ile Cys Arg Val Asn Arg Asn Ser Gly Ser Cys Leu Gly	
	180 185 190 195 200 205	

290																	
	Gly	Asp	Glu	Ile	Phe	Leu	Leu	Cys	Asp	Lys	Val	Gln	Lys	Glu	Asp	Ile	
	210						215					220					
5	GAG	GTG	TAT	TTC	ACG	GGA	CCA	GGC	TGG	GAG	GCC	CGA	GGC	TCC	TTT	TCG	720
	Glu	Val	Tyr	Phe	Thr	Gly	Pro	Gly	Trp	Glu	Ala	Arg	Gly	Ser	Phe	Ser	
	225					230				235						240	
10	CAA	GCT	GAT	GTG	CAC	CGA	CAA	GTG	GCC	ATT	GTG	TTC	CGG	ACC	CCT	CCC	768
	Gln	Ala	Asp	Val	His	Arg	Gln	Val	Ala	Ile	Val	Phe	Arg	Thr	Pro	Pro	
				245						250					255		
15	TAC	GCA	GAC	CCC	AGC	CTG	CAG	GCT	CCT	GTG	CGT	GTC	TCC	ATG	CAG	CTG	816
	Tyr	Ala	Asp	Pro	Ser	Leu	Gln	Ala	Pro	Val	Arg	Val	Ser	Met	Gln	Leu	
				260				265						270			
20	CGG	CGG	CCT	TCC	GAC	CGG	GAG	CTC	AGT	GAG	CCC	ATG	GAA	TTC	CAG	TAC	864
	Arg	Arg	Pro	Ser	Asp	Arg	Glu	Leu	Ser	Glu	Pro	Met	Glu	Phe	Gln	Tyr	
			275					280				285					
25	CTG	CCA	GAT	ACA	GAC	GAT	CGT	CAC	CGG	ATT	GAG	GAG	AAA	CGT	AAA	AGG	912
	Leu	Pro	Asp	Thr	Asp	Asp	Arg	His	Arg	Ile	Glu	Glu	Lys	Arg	Lys	Arg	
	290						295					300					
30	ACA	TAT	GAG	ACC	TTC	AAG	AGC	ATC	ATG	AAG	AAG	AGT	CCT	TTC	AGC	GGA	960
	Thr	Tyr	Glu	Thr	Phe	Lys	Ser	Ile	Met	Lys	Lys	Ser	Pro	Phe	Ser	Gly	
	305					310					315					320	
35	CCC	ACC	GAC	CCC	CGG	CCT	CCA	CCT	CGA	CGC	ATT	GCT	GTG	CCT	TCC	CGC	1008
	Pro	Thr	Asp	Pro	Arg	Pro	Pro	Pro	Arg	Arg	Ile	Ala	Val	Pro	Ser	Arg	
					325					330					335		
40	AGC	TCA	GCT	TCT	GTC	CCC	AAG	CCA	GCA	CCC	CAG	CCC	TAT	CCC	TTT	ACG	1056
	Ser	Ser	Ala	Ser	Val	Pro	Lys	Pro	Ala	Pro	Gln	Pro	Tyr	Pro	Phe	Thr	
				340				345						350			
45	TCA	TCC	CTG	AGC	ACC	ATC	AAC	TAT	GAT	GAG	TTT	CCC	ACC	ATG	GTG	TTT	1104
	Ser	Ser	Leu	Ser	Thr	Ile	Asn	Tyr	Asp	Glu	Phe	Pro	Thr	Met	Val	Phe	
			355				360						365				
50	CCT	TCT	GGG	CAG	ATC	AGC	CAG	GCC	TCG	GCC	TTG	GCC	CCG	GCC	CCT	CCC	1152
	Pro	Ser	Gly	Gln	Ile	Ser	Gln	Ala	Ser	Ala	Leu	Ala	Pro	Ala	Pro	Pro	
	370						375					380					
55	CAA	GTC	CTG	CCC	CAG	GCT	CCA	GCC	CCT	GCC	CCT	GCT	CCA	GCC	ATG	GTA	1200
	Gln	Val	Leu	Pro	Gln	Ala	Pro	Ala	Pro	Ala	Pro	Ala	Pro	Ala	Met	Val	
	385					390					395					400	
60	CGT	GGT	CAG	GAT	GTG	CCC	CCA	CCT	GGC	CCC	AAG	CCC	ACC	CAG	GCT	GGC	1296
	Pro	Pro	Gln	Ala	Val	Ala	Pro	Pro	Ala	Pro	Lys	Pro	Thr	Gln	Ala	Gly	
				420					425					430			

291

	Glu	Gly	Thr	Leu	Ser	Glu	Ala	Leu	Leu	Gln	Leu	Gln	Phe	Asp	Asp	Glu	
			435					440					445				
5	GAC	CTG	GGG	GCC	TTG	CTT	GGC	AAC	AGC	ACA	GAC	CCA	GCT	GTG	TTC	ACA	1392
	Asp	Leu	Gly	Ala	Leu	Leu	Gly	Asn	Ser	Thr	Asp	Pro	Ala	Val	Phe	Thr	
		450					455					460					
10	GAC	CTG	GCA	TCC	GTC	GAC	AAC	TCC	GAG	TTT	CAG	CAG	CTG	CTG	AAC	CAG	1440
	Asp	Leu	Ala	Ser	Val	Asp	Asn	Ser	Glu	Phe	Gln	Gln	Leu	Leu	Asn	Gln	
		465					470				475					480	
15	GGC	ATA	CCT	GTG	GCC	CCC	CAC	ACA	ACT	GAG	CCC	ATG	CTG	ATG	GAG	TAC	1488
	Gly	Ile	Pro	Val	Ala	Pro	His	Thr	Thr	Glu	Pro	Met	Leu	Met	Glu	Tyr	
					485					490					495		
	CCT	GAG	GCT	ATA	ACT	CGC	CTA	GTG	ACA	GGG	GCC	CAG	AGG	CCC	CCC	GAC	1536
	Pro	Glu	Ala	Ile	Thr	Arg	Leu	Val	Thr	Gly	Ala	Gln	Arg	Pro	Pro	Asp	
				500					505					510			
20	CCA	GCT	CCT	GCT	CCA	CTG	GGG	GCC	CCG	GGG	CTC	CCC	AAT	GGC	CTC	CTT	1584
	Pro	Ala	Pro	Ala	Pro	Leu	Gly	Ala	Pro	Gly	Leu	Pro	Asn	Gly	Leu	Leu	
			515					520					525				
25	TCA	GGA	GAT	GAA	GAC	TTC	TCC	TCC	ATT	GCG	GAC	ATG	GAC	TTC	TCA	GCC	1632
	Ser	Gly	Asp	Glu	Asp	Phe	Ser	Ser	Ile	Ala	Asp	Met	Asp	Phe	Ser	Ala	
		530						535				540					
30	CTG	CTG	AGT	CAG	ATC	AGC	TCC	TTG	GAT	CCA	CCG	GTC	GCC	ACC	ATG	GTG	1680
	Leu	Leu	Ser	Gln	Ile	Ser	Ser	Leu	Asp	Pro	Pro	Val	Ala	Thr	Met	Val	
		545					550				555					560	
35	AGC	AAG	GGC	GAG	GAG	CTG	TTC	ACC	GGG	GTG	GTG	CCC	ATC	CTG	GTC	GAG	1728
	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	Val	Glu	
					565					570					575		
	CTG	GAC	GGC	GAC	GTA	AAC	GGC	CAC	AAG	TTC	AGC	GTG	TCC	GGC	GAG	GGC	1776
	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	Glu	Gly	
					580				585					590			
40	GAG	GGC	GAT	GCC	ACC	TAC	GGC	AAG	CTG	ACC	CTG	AAG	TTC	ATC	TGC	ACC	1824
	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	Cys	Thr	
			595					600					605				
45	ACC	GGC	AAG	CTG	CCC	GTG	CCC	TGG	CCC	ACC	CTC	GTG	ACC	ACC	CTG	ACC	1872
	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	Leu	Thr	
		610					615					620					
55	TAC	GAC	GTC	GAG	TTC	TTG	AAC	GGC	TTT	CAG	CAG	CTG	CTG	AAC	CAG		
	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	Arg	Thr	
					645						650				655		

292

	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	Val	Lys	
				660				665						670			
5	TTC	GAG	GGC	GAC	ACC	CTG	GTG	AAC	CGC	ATC	GAG	CTG	AAG	GGC	ATC	GAC	2064
	Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	Ile	Asp	
			675					680					685				
10	TTC	AAG	GAG	GAC	GGC	AAC	ATC	CTG	GGG	CAC	AAG	CTG	GAG	TAC	AAC	TAC	2112
	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	Asn	Tyr	
		690					695					700					
15	AAC	AGC	CAC	AAC	GTC	TAT	ATC	ATG	GCC	GAC	AAG	CAG	AAG	AAC	GGC	ATC	2160
	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	Gly	Ile	
	705					710					715				720		
	AAG	GTG	AAC	TTC	AAG	ATC	CGC	CAC	AAC	ATC	GAG	GAC	GGC	AGC	GTG	CAG	2208
	Lys	Val	Asn	Phe	Lys	Ile	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	Val	Gln	
					725					730					735		
20	CTC	GCC	GAC	CAC	TAC	CAG	CAG	AAC	ACC	CCC	ATC	GGC	GAC	GGC	CCC	GTG	2256
	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	Pro	Val	
				740					745					750			
25	CTG	CTG	CCC	GAC	AAC	CAC	TAC	CTG	AGC	ACC	CAG	TCC	GCC	CTG	AGC	AAA	2304
	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	Ser	Lys	
			755					760					765				
30	GAC	CCC	AAC	GAG	AAG	CGC	GAT	CAC	ATG	GTC	CTG	CTG	GAG	TTC	GTG	ACC	2352
	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	Val	Thr	
		770					775					780					
35	GCC	GCC	GGG	ATC	ACT	CTC	GGC	ATG	GAC	GAG	CTG	TAC	AAG	TAA			2394
	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys				
	785					790					795						

(2) INFORMATION FOR SEQ ID NO:141:

- (i) SEQUENCE CHARACTERISTICS:
- 40 (A) LENGTH: 797 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- 45 (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal

Arg Gly Glu Tyr Val Gln Ile Ile Glu Gln Pro Lys Gln Arg Gly Met
20 25 30

Arg Phe Arg Tyr Lys Cys Glu Gly Arg Ser Ala Gly Ser Ile Pro Gly
35 40 45

[illegible]

55 Asp Leu Ala Ser Val Asp Asn Ser Glu Phe Glu Glu Leu Leu Asn Glu
465 470 475 480
Gly Ile Pro Val Ala Pro His Thr Thr Glu Pro Met Leu Met Glu Tyr
485 490 495

[illegible]

40

45

55

	Met	Val	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	
	1				5					10					15		
5	GTC Val	GAG Glu	CTG Leu	GAC Asp	GGC Gly	GAC Asp	GTA Val	AAC Asn	GGC Gly	CAC His	AAG Lys	TTC Phe	AGC Ser	GTG Val	TCC Ser	GGC Gly	96
				20					25					30			
10	GAG Glu	GGC Gly	GAG Glu	GGC Gly	GAT Asp	GCC Ala	ACC Thr	TAC Tyr	GGC Gly	AAG Lys	CTG Leu	ACC Thr	CTG Leu	AAG Lys	TTC Phe	ATC Ile	144
				35				40						45			
15	TGC Cys	ACC Thr	ACC Thr	GGC Gly	AAG Lys	CTG Leu	CCC Pro	GTG Val	CCC Pro	TGG Trp	CCC Pro	ACC Thr	CTC Leu	GTG Val	ACC Thr	ACC Thr	192
				50			55						60				
20	CTG Leu	ACC Thr	TAC Tyr	GGC Gly	GTG Val	CAG Gln	TGC Cys	TTC Phe	AGC Ser	CGC Arg	TAC Tyr	CCC Pro	GAC Asp	CAC His	ATG Met	AAG Lys	240
	65					70				75						80	
25	CAG Gln	CAC His	GAC Asp	TTC Phe	TTC Phe	AAG Lys	TCC Ser	GCC Ala	ATG Met	CCC Pro	GAA Glu	GGC Gly	TAC Tyr	GTC Val	CAG Gln	GAG Glu	288
					85					90					95		
30	CGC Arg	ACC Thr	ATC Ile	TTC Phe	TTC Phe	AAG Lys	GAC Asp	GAC Asp	GGC Gly	AAC Asn	TAC Tyr	AAG Lys	ACC Thr	CGC Arg	GCC Ala	GAG Glu	336
				100					105					110			
35	GTG Val	AAG Lys	TTC Phe	GAG Glu	GGC Gly	GAC Asp	ACC Thr	CTG Leu	GTG Val	AAC Asn	CGC Arg	ATC Ile	GAG Glu	CTG Leu	AAG Lys	GGC Gly	384
				115				120					125				
40	ATC Ile	GAC Asp	TTC Phe	AAG Lys	GAG Glu	GAC Asp	GGC Gly	AAC Asn	ATC Ile	CTG Leu	GGG Gly	CAC His	AAG Lys	CTG Leu	GAG Glu	TAC Tyr	432
				130			135						140				
45	AAC Asn	TAC Tyr	AAC Asn	AGC Ser	CAC His	AAC Asn	GTC Val	TAT Tyr	ATC Ile	ATG Met	GCC Ala	GAC Asp	AAG Lys	CAG Gln	AAG Lys	AAC Asn	480
	145					150					155					160	
50	GGC Gly	ATC Ile	AAG Lys	GTG Val	AAC Asn	TTC Phe	AAG Lys	ATC Ile	CGC Arg	CAC His	AAC Asn	ATC Ile	GAG Glu	GAC Asp	GGC Gly	AGC Ser	528
					165				170						175		
55	GTG Val	CAG Gln	CTC Leu	GCC Ala	GAC Asp	CAC His	TAC Tyr	CAG Gln	CAG Gln	AAC Asn	ACC Thr	CCC Pro	ATC Ile	GGC Gly	GAC Asp	GGC Gly	576
				180					185					190			
60	TGC Cys	ACC Thr	ACC Thr	GGC Gly	AAG Lys	CTG Leu	CCC Pro	GTG Val	CCC Pro	TGG Trp	CCC Pro	ACC Thr	CTC Leu	GTG Val	ACC Thr	ACC Thr	624
				200					205					210			
65	CTG Leu	ACC Thr	TAC Tyr	GGC Gly	GTG Val	CAG Gln	TGC Cys	TTC Phe	AGC Ser	CGC Arg	TAC Tyr	CCC Pro	GAC Asp	CAC His	ATG Met	AAG Lys	672
	215					220										225	
70	ATC Ile	GAC Asp	TTC Phe	AAG Lys	GAG Glu	GAC Asp	GGC Gly	AAC Asn	ATC Ile	CTG Leu	GGG Gly	CAC His	AAG Lys	CTG Leu	GAG Glu	TAC Tyr	720
				230			235						240				

296

	Val	Thr	Ala	Ala	Gly	Ile	Thr	Leu	Gly	Met	Asp	Glu	Leu	Tyr	Lys	Ser	
	225					230					235					240	
5	GGA	CTC	AGA	TCT	CGA	GCC	ATG	GAC	GAA	CTG	TTC	CCC	CTC	ATC	TTC	CCG	768
	Gly	Leu	Arg	Ser	Arg	Ala	Met	Asp	Glu	Leu	Phe	Pro	Leu	Ile	Phe	Pro	
					245					250					255		
10	GCA	GAG	CCA	GCC	CAG	GCC	TCT	GGC	CCC	TAT	GTG	GAG	ATC	ATT	GAG	CAG	816
	Ala	Glu	Pro	Ala	Gln	Ala	Ser	Gly	Pro	Tyr	Val	Glu	Ile	Ile	Glu	Gln	
				260					265					270			
15	CCC	AAG	CAG	CGG	GGC	ATG	CGC	TTC	CGC	TAC	AAG	TGC	GAG	GGG	CGC	TCC	864
	Pro	Lys	Gln	Arg	Gly	Met	Arg	Phe	Arg	Tyr	Lys	Cys	Glu	Gly	Arg	Ser	
			275					280					285				
20	GCG	GGC	AGC	ATC	CCA	GGC	GAG	AGG	AGC	ACA	GAT	ACC	ACC	AAG	ACC	CAC	912
	Ala	Gly	Ser	Ile	Pro	Gly	Glu	Arg	Ser	Thr	Asp	Thr	Thr	Lys	Thr	His	
			290					295				300					
25	CCC	ACC	ATC	AAG	ATC	AAT	GGC	TAC	ACA	GGA	CCA	GGG	ACA	GTG	CGC	ATC	960
	Pro	Thr	Ile	Lys	Ile	Asn	Gly	Tyr	Thr	Gly	Pro	Gly	Thr	Val	Arg	Ile	
	305					310					315					320	
30	TCC	CTG	GTC	ACC	AAG	GAC	CCT	CCT	CAC	CGG	CCT	CAC	CCC	CAC	GAG	CTT	1008
	Ser	Leu	Val	Thr	Lys	Asp	Pro	Pro	His	Arg	Pro	His	Pro	His	Glu	Leu	
					325					330					335		
35	GTA	GGA	AAG	GAC	TGC	CGG	GAT	GGC	TTC	TAT	GAG	GCT	GAG	CTC	TGC	CCG	1056
	Val	Gly	Lys	Asp	Cys	Arg	Asp	Gly	Phe	Tyr	Glu	Ala	Glu	Leu	Cys	Pro	
				340					345					350			
40	GAC	CGC	TGC	ATC	CAC	AGT	TTC	CAG	AAC	CTG	GGA	ATC	CAG	TGT	GTG	AAG	1104
	Asp	Arg	Cys	Ile	His	Ser	Phe	Gln	Asn	Leu	Gly	Ile	Gln	Cys	Val	Lys	
			355					360					365				
45	AAG	CGG	GAC	CTG	GAG	CAG	GCT	ATC	AGT	CAG	CGC	ATC	CAG	ACC	AAC	AAC	1152
	Lys	Arg	Asp	Leu	Glu	Gln	Ala	Ile	Ser	Gln	Arg	Ile	Gln	Thr	Asn	Asn	
			370				375					380					
50	AAC	CCC	TTC	CAA	GTT	CCT	ATA	GAA	GAG	CAG	CGT	GGG	GAC	TAC	GAC	CTG	1200
	Asn	Pro	Phe	Gln	Val	Pro	Ile	Glu	Glu	Gln	Arg	Gly	Asp	Tyr	Asp	Leu	
	385					390					395					400	
55	AAT	GCT	GTG	CGG	CTC	TGC	TTC	CAG	GTG	ACA	GTG	CGG	GAC	CCA	TCA	GGC	1248
	Asn	Ala	Val	Arg	Leu	Cys	Phe	Gln	Val	Thr	Val	Arg	Asp	Pro	Ser	Gly	
				405						410						415	
60	GGT	CCC	CCC	AAC	AGT	GCC	GAG	CTC	AAG	ATC	TGC	CGA	GTG	AAC	CGA	AAC	1344
	Arg	Ala	Pro	Asn	Thr	Ala	Glu	Leu	Lys	Ile	Cys	Arg	Val	Asn	Arg	Asn	
			435					440					445				

297

	Ser	Gly	Ser	Cys	Leu	Gly	Gly	Asp	Glu	Ile	Phe	Leu	Leu	Cys	Asp	Lys	
	450						455					460					
5	GTG	CAG	AAA	GAG	GAC	ATT	GAG	GTG	TAT	TTC	ACG	GGA	CCA	GGC	TGG	GAG	1440
	Val	Gln	Lys	Glu	Asp	Ile	Glu	Val	Tyr	Phe	Thr	Gly	Pro	Gly	Trp	Glu	
	465					470					475					480	
10	GCC	CGA	GGC	TCC	TTT	TCG	CAA	GCT	GAT	GTG	CAC	CGA	CAA	GTG	GCC	ATT	1488
	Ala	Arg	Gly	Ser	Phe	Ser	Gln	Ala	Asp	Val	His	Arg	Gln	Val	Ala	Ile	
					485					490					495		
15	GTG	TTC	CGG	ACC	CCT	CCC	TAC	GCA	GAC	CCC	AGC	CTG	CAG	GCT	CCT	GTG	1536
	Val	Phe	Arg	Thr	Pro	Pro	Tyr	Ala	Asp	Pro	Ser	Leu	Gln	Ala	Pro	Val	
				500					505					510			
20	CGT	GTC	TCC	ATG	CAG	CTG	CGG	CGG	CCT	TCC	GAC	CGG	GAG	CTC	AGT	GAG	1584
	Arg	Val	Ser	Met	Gln	Leu	Arg	Arg	Pro	Ser	Asp	Arg	Glu	Leu	Ser	Glu	
			515					520					525				
25	CCC	ATG	GAA	TTC	CAG	TAC	CTG	CCA	GAT	ACA	GAC	GAT	CGT	CAC	CGG	ATT	1632
	Pro	Met	Glu	Phe	Gln	Tyr	Leu	Pro	Asp	Thr	Asp	Asp	Arg	His	Arg	Ile	
		530					535					540					
30	GAG	GAG	AAA	CGT	AAA	AGG	ACA	TAT	GAG	ACC	TTC	AAG	AGC	ATC	ATG	AAG	1680
	Glu	Glu	Lys	Arg	Lys	Arg	Thr	Tyr	Glu	Thr	Phe	Lys	Ser	Ile	Met	Lys	
	545					550					555					560	
35	AAG	AGT	CCT	TTC	AGC	GGA	CCC	ACC	GAC	CCC	CGG	CCT	CCA	CCT	CGA	CGC	1728
	Lys	Ser	Pro	Phe	Ser	Gly	Pro	Thr	Asp	Pro	Arg	Pro	Pro	Pro	Arg	Arg	
					565					570					575		
40	ATT	GCT	GTG	CCT	TCC	CGC	AGC	TCA	GCT	TCT	GTG	CCC	AAG	CCA	GCA	CCC	1776
	Ile	Ala	Val	Pro	Ser	Arg	Ser	Ser	Ala	Ser	Val	Pro	Lys	Pro	Ala	Pro	
				580					585					590			
45	CAG	CCC	TAT	CCC	TTT	ACG	TCA	TCC	CTG	AGC	ACC	ATC	AAC	TAT	GAT	GAG	1824
	Gln	Pro	Tyr	Pro	Phe	Thr	Ser	Ser	Leu	Ser	Thr	Ile	Asn	Tyr	Asp	Glu	
			595					600					605				
50	TTT	CCC	ACC	ATG	GTG	TTT	CCT	TCT	GGG	CAG	ATC	AGC	CAG	GCC	TCG	GCC	1872
	Phe	Pro	Thr	Met	Val	Phe	Pro	Ser	Gly	Gln	Ile	Ser	Gln	Ala	Ser	Ala	
		610					615					620					
55	TTG	GCC	CCG	GCC	CCT	CCC	CAA	GTC	CTG	CCC	CAG	GCT	CCA	GCC	CCT	GCC	1920
	Leu	Ala	Pro	Ala	Pro	Pro	Gln	Val	Leu	Pro	Gln	Ala	Pro	Ala	Pro	Ala	
	625					630					635					640	
60	GGT	GCT	GAA	GGA	GAT	GAT	GAT	GAT	GAT	GAT	GAT	GAT	GAT	GAT	GAT	GAT	2016
	Pro	Val	Leu	Ala	Pro	Gly	Pro	Pro	Gln	Ala	Val	Ala	Pro	Pro	Ala	Pro	
				660					665					670			

298

	Lys	Pro	Thr	Gln	Ala	Gly	Glu	Gly	Thr	Leu	Ser	Glu	Ala	Leu	Leu	Gln	
			675					680					685				
5	CTG	CAG	TTT	GAT	GAT	GAA	GAC	CTG	GGG	GCC	TTG	CTT	GGC	AAC	AGC	ACA	2112
	Leu	Gln	Phe	Asp	Asp	Glu	Asp	Leu	Gly	Ala	Leu	Leu	Gly	Asn	Ser	Thr	
			690				695					700					
10	GAC	CCA	GCT	GTG	TTC	ACA	GAC	CTG	GCA	TCC	GTC	GAC	AAC	TCC	GAG	TTT	2160
	Asp	Pro	Ala	Val	Phe	Thr	Asp	Leu	Ala	Ser	Val	Asp	Asn	Ser	Glu	Phe	
			705			710					715				720		
15	CAG	CAG	CTG	CTG	AAC	CAG	GGC	ATA	CCT	GTG	GCC	CCC	CAC	ACA	ACT	GAG	2208
	Gln	Gln	Leu	Leu	Asn	Gln	Gly	Ile	Pro	Val	Ala	Pro	His	Thr	Thr	Glu	
					725				730						735		
	CCC	ATG	CTG	ATG	GAG	TAC	CCT	GAG	GCT	ATA	ACT	CGC	CTA	GTG	ACA	GGG	2256
	Pro	Met	Leu	Met	Glu	Tyr	Pro	Glu	Ala	Ile	Thr	Arg	Leu	Val	Thr	Gly	
				740				745					750				
20	GCC	CAG	AGG	CCC	CCC	GAC	CCA	GCT	CCT	GCT	CCA	CTG	GGG	GCC	CCG	GGG	2304
	Ala	Gln	Arg	Pro	Pro	Asp	Pro	Ala	Pro	Ala	Pro	Leu	Gly	Ala	Pro	Gly	
			755				760						765				
25	CTC	CCC	AAT	GGC	CTC	CTT	TCA	GGA	GAT	GAA	GAC	TTC	TCC	TCC	ATT	GCG	2352
	Leu	Pro	Asn	Gly	Leu	Leu	Ser	Gly	Asp	Glu	Asp	Phe	Ser	Ser	Ile	Ala	
		770				775					780						
30	GAC	ATG	GAC	TTC	TCA	GCC	CTG	CTG	AGT	CAG	ATC	AGC	TCC	TAA			2394
	Asp	Met	Asp	Phe	Ser	Ala	Leu	Leu	Ser	Gln	Ile	Ser	Ser				
		785				790				795							

(2) INFORMATION FOR SEQ ID NO:143:

35	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 797 amino acids	
	(B) TYPE: amino acid	
	(C) STRANDEDNESS: single	
	(D) TOPOLOGY: linear	
40	(ii) MOLECULE TYPE: protein	
	(v) FRAGMENT TYPE: internal	
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:	
	Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu	
	1 5 10 15	

55	Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr	
	50 55 60	
	Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys	
	65 70 75 80	

SUBSTITUTE SHEET (RULE 26)

300

		530			535			540									
		Glu	Glu	Lys	Arg	Lys	Arg	Thr	Tyr	Glu	Thr	Phe	Lys	Ser	Ile	Met	Lys
		545					550					555					560
		Lys	Ser	Pro	Phe	Ser	Gly	Pro	Thr	Asp	Pro	Arg	Pro	Pro	Pro	Arg	Arg
5						565					570					575	
		Ile	Ala	Val	Pro	Ser	Arg	Ser	Ser	Ala	Ser	Val	Pro	Lys	Pro	Ala	Pro
					580					585					590		
		Gln	Pro	Tyr	Pro	Phe	Thr	Ser	Ser	Leu	Ser	Thr	Ile	Asn	Tyr	Asp	Glu
				595					600					605			
10		Phe	Pro	Thr	Met	Val	Phe	Pro	Ser	Gly	Gln	Ile	Ser	Gln	Ala	Ser	Ala
				610					615					620			
		Leu	Ala	Pro	Ala	Pro	Pro	Gln	Val	Leu	Pro	Gln	Ala	Pro	Ala	Pro	Ala
				625			630					635					640
		Pro	Ala	Pro	Ala	Met	Val	Ser	Ala	Leu	Ala	Gln	Ala	Pro	Ala	Pro	Val
15					645						650					655	
		Pro	Val	Leu	Ala	Pro	Gly	Pro	Pro	Gln	Ala	Val	Ala	Pro	Pro	Ala	Pro
				660					665					670			
		Lys	Pro	Thr	Gln	Ala	Gly	Glu	Gly	Thr	Leu	Ser	Glu	Ala	Leu	Leu	Gln
				675					680					685			
20		Leu	Gln	Phe	Asp	Asp	Glu	Asp	Leu	Gly	Ala	Leu	Leu	Gly	Asn	Ser	Thr
				690				695						700			
		Asp	Pro	Ala	Val	Phe	Thr	Asp	Leu	Ala	Ser	Val	Asp	Asn	Ser	Glu	Phe
				705			710					715					720
		Gln	Gln	Leu	Leu	Asn	Gln	Gly	Ile	Pro	Val	Ala	Pro	His	Thr	Thr	Glu
25					725						730					735	
		Pro	Met	Leu	Met	Glu	Tyr	Pro	Glu	Ala	Ile	Thr	Arg	Leu	Val	Thr	Gly
				740					745					750			
		Ala	Gln	Arg	Pro	Pro	Asp	Pro	Ala	Pro	Ala	Pro	Leu	Gly	Ala	Pro	Gly
				755				760					765				
30		Leu	Pro	Asn	Gly	Leu	Leu	Ser	Gly	Asp	Glu	Asp	Phe	Ser	Ser	Ile	Ala
				770				775					780				
		Asp	Met	Asp	Phe	Ser	Ala	Leu	Leu	Ser	Gln	Ile	Ser	Ser			
				785			790					795					

CLAIMS

1. A method for extracting quantitative information relating to an influence on a cellular re-
sponse, the method comprising recording variation, caused by the influence on a mechani-
cally intact living cell or mechanically intact living cells, in spatially distributed light emitted
5 from a luminophore, the luminophore being present in the cell or cells and being capable of
being redistributed in a manner which is related with the degree of the influence, and/or of
being modulated by a component which is capable of being redistributed in a manner which
is related to the degree of the influence, the association resulting in a modulation of the lu-
minescence characteristics of the luminophore, and processing the recorded variation in the
10 spatially distributed light to provide quantitative information correlating the spatial distribution
to the degree of the influence on the cellular response.

2. A method according to claim 1, as used for extracting quantitative information relating to
15 an influence on an intracellular pathway involving redistribution of at least one component
associated with the pathway, or part thereof, the method comprising recording the result of
the influence on mechanically intact living cell or cells, as manifested in spatially distributed
light emitted from a luminophore which is present in the cell or cells and which is capable of
being redistributed, by modulation of the pathway, in a manner which is related to the redis-
tribution of the at least one component of the intracellular pathway, processing the recorded
20 result to provide quantitative information about the spatially distributed light and correlating
the quantitative information to the degree of the influence on the intracellular pathway.

3. A method according to claim 1 or 2, wherein the quantitative information which is indica-
25 tive of the degree of the cellular response to the influence or the result of the influence on
the intracellular pathway is extracted from the recording or recordings according to a prede-
termined calibration based on responses or results, recorded in the same manner, to known

30 4. A method according to any of the preceding claims, wherein the influence is contact be-
tween the mechanically intact living cell or the group of mechanically intact living cells with a

chemical substance and/or incubation of the mechanically intact living cell or the group of mechanically intact living cells with a chemical substance.

- 5 5. A method according to claim 4 wherein the substance is a substance whose effect on an intracellular pathway is to be determined.
6. A method according to any of the preceding claims, wherein the recording is made at a single point in time after the application of the influence.
- 10 7. A method according to any of claims 1-5, wherein the recording is made at two points in time, one point being before, and the other point being after the application of the influence.
8. A method according to any of claims 1-5, wherein the recording is performed at a series of points in time, in which the application of the influence occurs at some time after the first
15 time point in the series of recordings, the recording being performed, e.g., with a predetermined time spacing of from 0.1 seconds to 1 hour, preferably from 1 to 60 seconds, more preferably from 1 to 30 seconds, in particular from 1 to 10 seconds, over a time span of from 1 second to 12 hours, such as from 10 seconds to 12 hours, e.g., from 10 seconds to one hour, such as from 60 seconds to 30 minutes or 20 minutes.
- 20 9. A method according to any of claims 1-7, wherein the cell or cells is/are fixed at a point in time after the application of the influence at which the response has been predetermined to be significant, and the recording is made at an arbitrary later time.
- 25 10. A method according to any of the preceding claims, wherein the luminophore is a lu-

11. A method according to any of the preceding claims, wherein the luminophore is a luminophore which is capable of associating with a component which is capable of being redistributed in manner which is physiologically relevant to the degree of the influence.
- 5 12. A method according to any of the preceding claims, wherein the luminophore is a luminophore which is capable of being redistributed in a manner which is experimentally determined to be correlated to the degree of the influence.
- 10 13. A method according to any of the preceding claims, wherein the luminophore is a luminophore which is capable of being redistributed, by modulation of the intracellular pathway, in substantially the same manner as the at least one component of the intracellular pathway.
- 15 14. A method according to any of claims 1-13, wherein the luminophore is a luminophore which is capable of being quenched upon spatial association with a component which is redistributed by modulation of the pathway, the quenching being measured as a decrease in the intensity of the luminescence.
- 20 15. A method according to any of claims 1-13, wherein the variation or result with respect to the spatially distributed light emitted by the luminophore is detected by a change in the resonance energy transfer between the luminophore and another luminescent entity capable of delivering energy to the luminophore, each of which has been selected or engineered to become part of, bound to or associated with particular components of the intracellular pathway, and one of which undergoes redistribution in response to the influence, thereby changing the
25 amount of resonance energy transfer, the change in the resonance energy transfer being measured as a change in the intensity of emission from the luminophore.
- 30 method according to claim 15 wherein the change in the intensity of the emission from the luminophore is sensed by a single channel photodetector which responds only to the average intensity of the luminophore in a non-spatially resolved fashion

17. A method according to any of claims 1-16, wherein the property of the light being recorded is intensity, fluorescence lifetime, polarization, wavelength shift, or other property which is modulated as a result of the underlying cellular response.

5

18. A method according to any of claims 1-15 or 17, wherein the recording of the spatially distributed light is performed using a recording system which records the spatial distribution of a recordable property of the light in the form of an ordered array of values.

10 19. A method according to claim 18, wherein the recording of the spatial distribution of the recordable property of the light is performed using a charge transfer device such as a CCD array or a vacuum tube device such as a vidicon tube.

15 20. A method according to any of the preceding claims, wherein the light to be measured passes through a filter which selects the desired component of the light to be measured and rejects other components.

21. A method according to any of the preceding claims, wherein the recording of the spatial distribution of the recordable property of light is performed by fluorescence microscopy.

20

22. A method according to any of the preceding claims, wherein the recording of the variation or result with respect to light emitted from the luminophore is performed by recording the spatially distributed light as one or more digital images, and the processing of the recorded variation to reduce it to one or more numbers representative of the degree of redistribution
25 comprises a digital image processing procedure or combination of digital image processing

23. A method according to any of claims 2-22, wherein the intracellular pathway is an intracellular signalling pathway.

24. A method according to any of the preceding claims, wherein the luminophore is a fluorophore.
- 5 25. A method according to any of the preceding claims wherein the luminophore is a polypeptide encoded by and expressed from a nucleotide sequence harboured in the cell or cells.
- 10 26. A method according to any of the preceding claims, wherein the luminophore is a hybrid polypeptide comprising a fusion of at least a portion of each of two polypeptides one of which comprises a luminescent polypeptide and the other one of which comprises a biologically active polypeptide, as defined herein.
- 15 27. A method according to claim 26, wherein the luminescent polypeptide is a GFP as defined herein.
28. A method according to claim 27 wherein the GFP is selected from the group consisting of green fluorescent proteins having the F64L mutation as defined herein.
- 20 29. A method according to claim 28 wherein the GFP is a GFP variant selected from the group consisting of F64L-GFP, F64L-Y66H-GFP, F64L-S65T-GFP, and EGFP.
30. A method according to any of the previous claims for detecting intracellular translocation of a biologically active polypeptide affecting intracellular processes upon activation, the
25 method comprising
31. A method according to any of the previous claims for detecting intracellular translocation of a polypeptide comprising a GFP which is N- or C-terminally tagged, optionally through a linker, to a biologically active polypeptide under conditions permitting expression of the nucleotide sequence,

- b) modulating the activity of the biologically active polypeptide by incubating the cell or cells with a substance having biological activity and
- c) measuring the fluorescence produced by the incubated cell or cells and determining the result or variation with respect to the fluorescence, such result or variation being indicative of the translocation of a biologically active polypeptide in said cell.

31. A method according to claim 30, wherein the nucleotide sequence is a DNA sequence.

32. A method according to claim 30 or 31, wherein the modulation is an activation.

33. A method according to claim 30 or 31, wherein the modulation is a deactivation.

34. A method according to any of claims 30-33 wherein the fluorescence of the cell or cells is measured prior to the modulation, and the result or variation determined in step (c) is a change in fluorescence compared to the fluorescence measured prior to the modulation.

35. A method according to any of claims 30-34, wherein the intracellular processes are intracellular signalling pathways.

36. A method according to claim 34, wherein the change in fluorescence measured in step (c) comprises determining a change in the spatial distribution of the fluorescence.

37. A method according to any of the preceding claims wherein the mechanically intact living cell or cells is/are a mammalian cell/mammalian cells which, during the time period over

which the influence is observed, are kept at a temperature of about 37°C.

The method according to any of the preceding claims is preferably performed in a cell culture medium.

The method according to any of the preceding claims is most preferably performed at a temperature of about 37°C.

38. A method according to any of the preceding claims, wherein the at least one mechanically intact living cell is part of a matrix of identical or non-identical cells.

39. A method according to any of claims 1-36 and 38, wherein the cell or cells is/are selected from the group consisting of fungal cells, such as a yeast cell; invertebrate cells including insect cells; and vertebrate cells, such as mammalian cells.

40. A nucleic acid construct coding for a fusion polypeptide comprising a biologically active polypeptide that is a component of an intracellular signalling pathway, or a part thereof, and a GFP, with the proviso that the construct is not a construct coding for a fusion polypeptide in which the biologically active polypeptide is selected from the group consisting of PKC-alpha, PKC-gamma, and PKC-epsilon.

41. A nucleic acid construct coding for a fusion polypeptide comprising a biologically active polypeptide that is a component of an intracellular signalling pathway, or a part thereof, and an F64L mutant of GFP.

42. A nucleic acid construct according to claim 40 or 41, wherein the biologically active polypeptide is a protein kinase or a phosphatase.

43. A nucleic acid construct according to any of claims 40-42 wherein the GFP is N- or C-terminally tagged, optionally via a peptide linker, to the biologically active polypeptide or part thereof.

44. A nucleic acid construct according to any of claims 40, 41 and 43, wherein the biologi-

45. A nucleic acid construct according to any of claims 40, 41 and 43, wherein the biologically active polypeptide is a protein, or a part thereof, which is associated with the cytoskeletal network and which changes cellular localisation upon activation.
- 5 46. A nucleic acid construct according to any of claims 40-43, wherein the biologically active polypeptide is a protein kinase or a part thereof which changes cellular localisation upon activation.
- 10 47. A nucleic acid construct according to claim 46, wherein the protein kinase is a serine/threonine protein kinase or a part thereof capable of changing intracellular localisation upon activation.
48. A nucleic acid construct according to claim 46, wherein the protein kinase is a tyrosine protein kinase or a part thereof capable of changing intracellular localisation upon activation.
- 15 49. A nucleic acid construct according to claim 46, wherein the protein kinase is a phospholipid-dependent serine/threonine protein kinase or a part thereof capable of changing intracellular localisation upon activation.
- 20 50. A nucleic acid construct according to claim 46, wherein the protein kinase is a cAMP-dependent protein kinase or a part thereof capable of changing cellular localisation upon activation.
- 25 51. A nucleic acid construct according to claim 50 which codes for a PKAc-F64L-S65T-GFP fusion.
52. A nucleic acid construct according to claim 49, wherein the protein kinase is a cAMP-dependent protein kinase or a part thereof capable of changing cellular localisation upon activation.

53. A nucleic acid construct according to claim 46, wherein the protein kinase is a calmodulin-dependent serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

5

54. A nucleic acid construct according to claim 46, wherein the protein kinase is a mitogen-activated serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

10 55. A nucleic acid construct according to claim 54, which codes for an ERK1-F64L-S65T-GFP fusion.

56. A nucleic acid construct according to claim 54, which codes for an EGFP-ERK1 fusion.

15 57. A nucleic acid construct according to claim 46, wherein the protein kinase is a cyclin-dependent serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

20 58. A nucleic acid construct according to claim 42 or 43, wherein the biologically active polypeptide is a protein phosphatase or a part thereof capable of changing cellular localisation upon activation.

59. A nucleic acid construct according to any of claims 40-58 which is a DNA construct.

60. A nucleic acid construct according to claim 59, wherein the gene encoding GFP is the gene encoding EGFP as defined herein.

61. A nucleic acid construct according to claim 60 in which the gene encoding GFP is the gene encoding EGFP as defined herein.

62. A nucleic acid construct according to claim 60 in which the gene encoding a GFP is a gene encoding a GFP variant selected from F64L-GFP, F64L-Y66H-GFP and F64L-S65T-GFP.

5

63. A DNA construct according to claim 59 and 61 or, where applicable, 62, which is a construct as identified by any of the DNA sequences shown in SEQ ID NO: 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, and 142, or is a variant thereof capable of encoding the same fusion polypeptide or a fusion polypeptide which is biologically equivalent thereto, as defined herein.

10

64. A cell containing a nucleic acid construct according to any of claims 40-63 and capable of expressing the sequence encoded by the construct.

15

65. A cell according to claim 64, which is a eukaryotic cell.

66. A cell according to claim 64, which is selected from the group consisting of fungal cells, such as yeast cells; invertebrate cells, including insect cells, and vertebrate cells, such as mammalian cells.

20

67. A cell according to claim 66, which is a mammalian cell.

68. An organism carrying in at least one of its component cells a nucleic acid sequence as contained in the constructs according to any of claims 40-59, said cell being capable of ex-

25

69. An organism according to claim 68 which is selected from the group consisting of unicellular and multicellular organisms, such as a mammal.

70. A fluorescent probe comprising a GFP which is N- or C-terminally tagged, optionally via a peptide linker, to a biologically active polypeptide or a part or a subunit thereof which is a component of an intracellular signalling pathway as defined herein, the probe being a probe
5 which is encoded by the nucleic acid construct according to any of claims 40-59.

71. A method according to any of claims 1-39, wherein the luminophore is a fusion polypeptide as encoded by the nucleic acid construct according to any of claims 40-63.

10 72. A method according to any of claims 1-39 or 71 in which the method of the invention is used in a screening program as defined herein.

73. An apparatus for measuring the distribution of fluorescence in at least one cell, and thereby any change in the distribution of fluorescence in at least one cell, which includes the
15 following component parts: (a) a light source, (b) a means for selecting the wavelength(s) of light from the source which will excite the fluorescence of the protein, (c) a means for rapidly blocking or passing the excitation light into the rest of the system, (d) a series of optical elements for conveying the excitation light to the specimen, collecting the emitted fluorescence in a spatially resolved fashion, and forming an image from this fluorescence, (e) a
20 bench or stand which holds the container of the cells being measured in a predetermined geometry with respect to the series of optical elements, (f) a detector to record the spatially resolved fluorescence in the form of an image, (g) a computer or electronic system and associated software to acquire and store the recorded images, and to compute the degree of redistribution from the recorded images.

25

74. An apparatus according to claim 73 in which some or all of the system is automated.

75. An apparatus according to claim 73 in which components d and e comprise a fluorescence microscope.

30

76. An apparatus according to claim 73 in which component f is a CCD camera.

77. An apparatus according to claim 73 in which the image is formed and recorded by an optical scanning system.

5

78. An apparatus according to claim 73 in which a liquid addition system is used to add a known or unknown compound to any or all of the cells in the cell holder at a time determined in advance.

10 79. An apparatus according to claim 78 in which the liquid addition system is under the control of the computer or electronic system.

80. A method according to any of claims 1-79 wherein the method is a screening program for the identification of a biologically active substance as defined herein that directly or indirectly affects an intracellular signalling pathway and is potentially useful as a medicament, wherein the result of the individual measurement of each substance being screened which indicates its potential biological activity is based on measurement of the redistribution of spatially resolved luminescence in living cells and which undergoes a change in distribution upon activation of an intracellular signalling pathway.

20

81 A method according to any of claims 1-79 wherein the method is a screening program for the identification of a biologically toxic substance as defined herein that exerts its toxic effect by interfering with an intracellular signalling pathway, wherein the result of the individual measurement of each substance being screened which indicates its potential biologically toxic activity is based on measurement of the redistribution of said fluorescent probe in living cells and which undergoes a change in distribution upon activation of an intracellular signal-

25

82. A method according to any of claims 1-80 wherein a fluorescent probe is used in back-tracking of signal transduction pathways as defined herein.

30

83. A method of treating a condition or disease related to the intracellular function of a protein kinase comprising administering to a patient suffering from said condition or disease an effective amount of a compound which has been discovered by any method according to the invention.

84. A compound that modulates a component of an intracellular pathway as defined herein, as determined by a method according to the method of the invention.

85. A medical composition comprising a therapeutic amount of a compound identified according to the method of the invention.

86. A method of selectively treating a patient suffering from an ailment which responds to medical treatment comprising obtaining a primary cell or cells from said patient, transfecting the cell or cells with at least one DNA sequence encoding a fluorescent probe according to the invention, culturing the cell or cells under conditions permitting the expression of said probes and exposing it to an array of medicaments suspected of being capable of alleviating said ailment, then comparing changes in fluorescence patterns or redistribution patterns of the fluorescent probes in the intact living cell or cells to detect the cellular response to the specific medicaments (obtaining a cellular action profile), then selecting a medicament(s) based on desired activity and acceptable level of side effects and administering an effective amount of said medicament(s) to said patient.

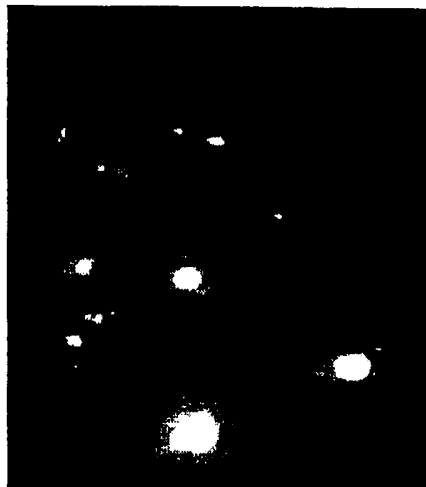
87. A method according to any of claims 1-80 of identifying a drug target among the group of biologically active polypeptides which are components of intracellular signalling pathways.

1 / 12

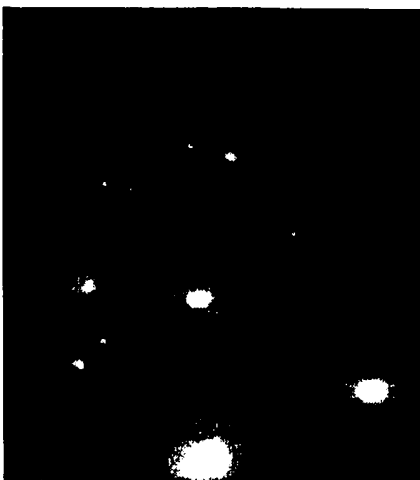
Fig 1



a)



b)



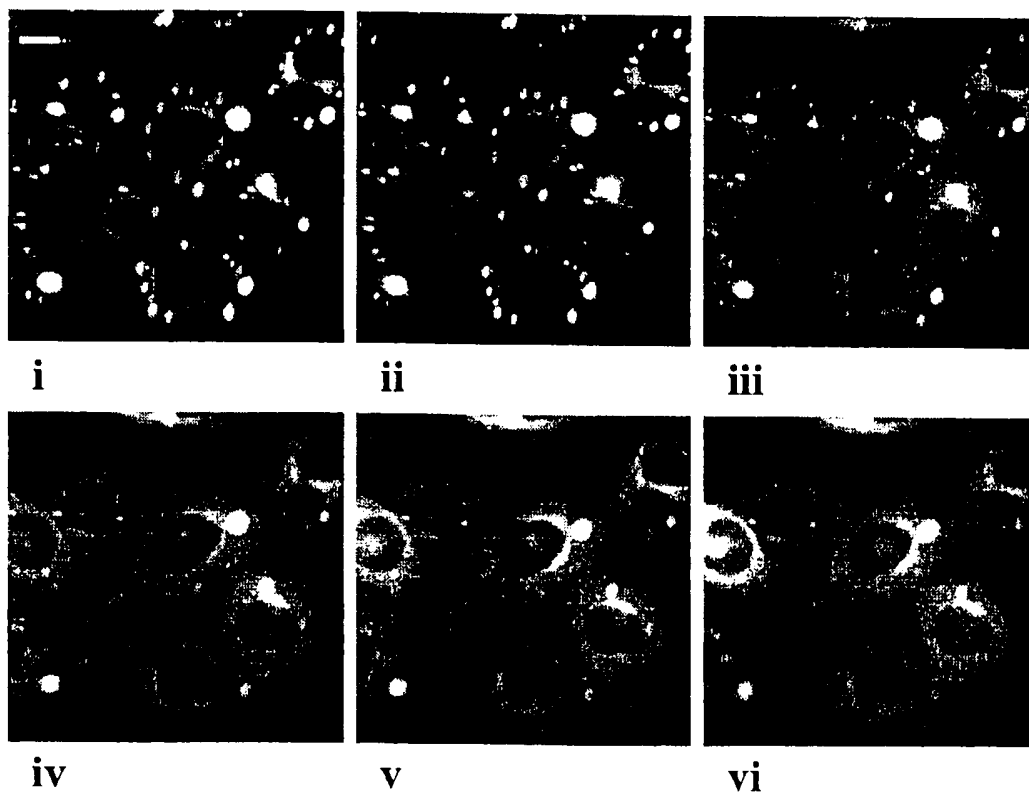
c)



d)

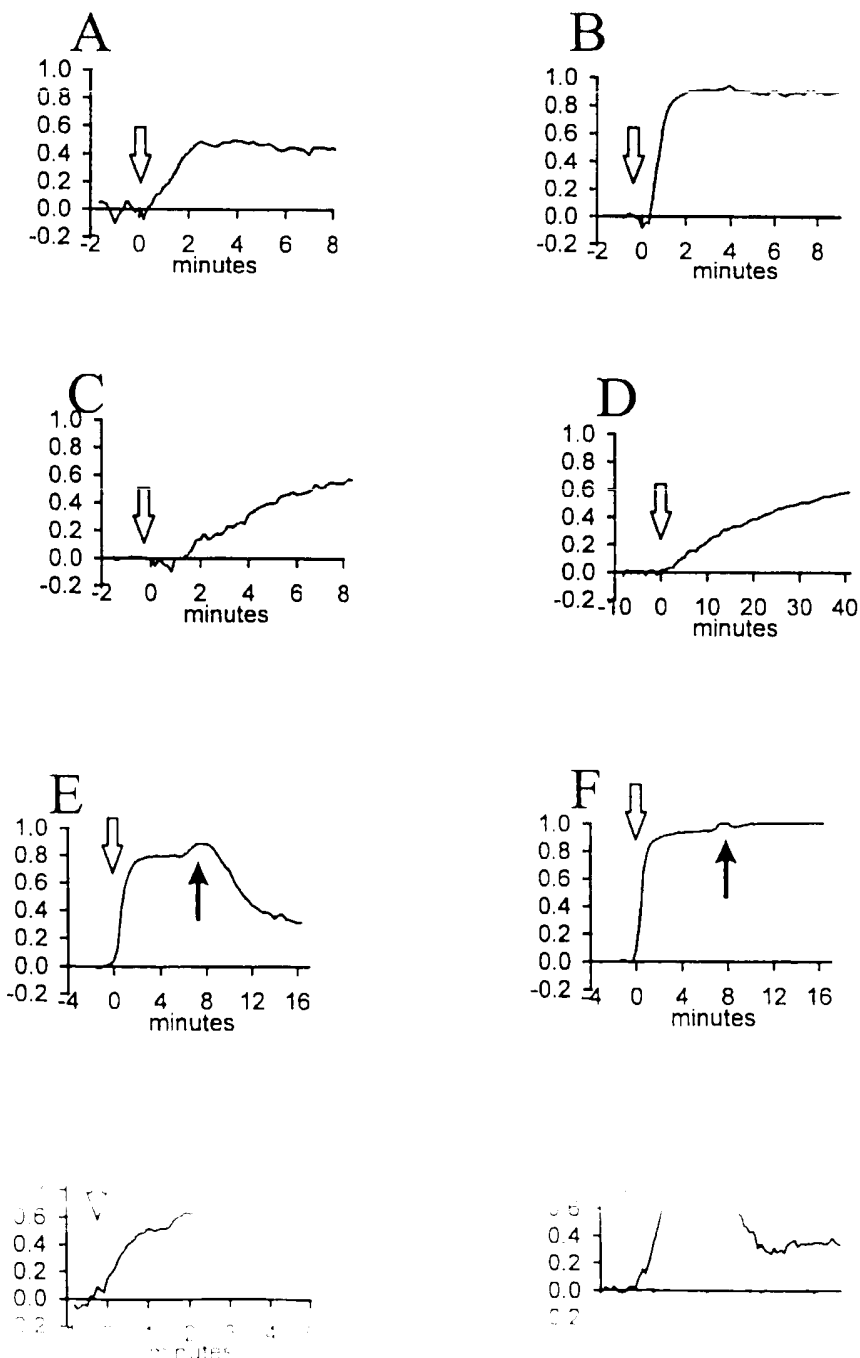
2/12

Fig 2



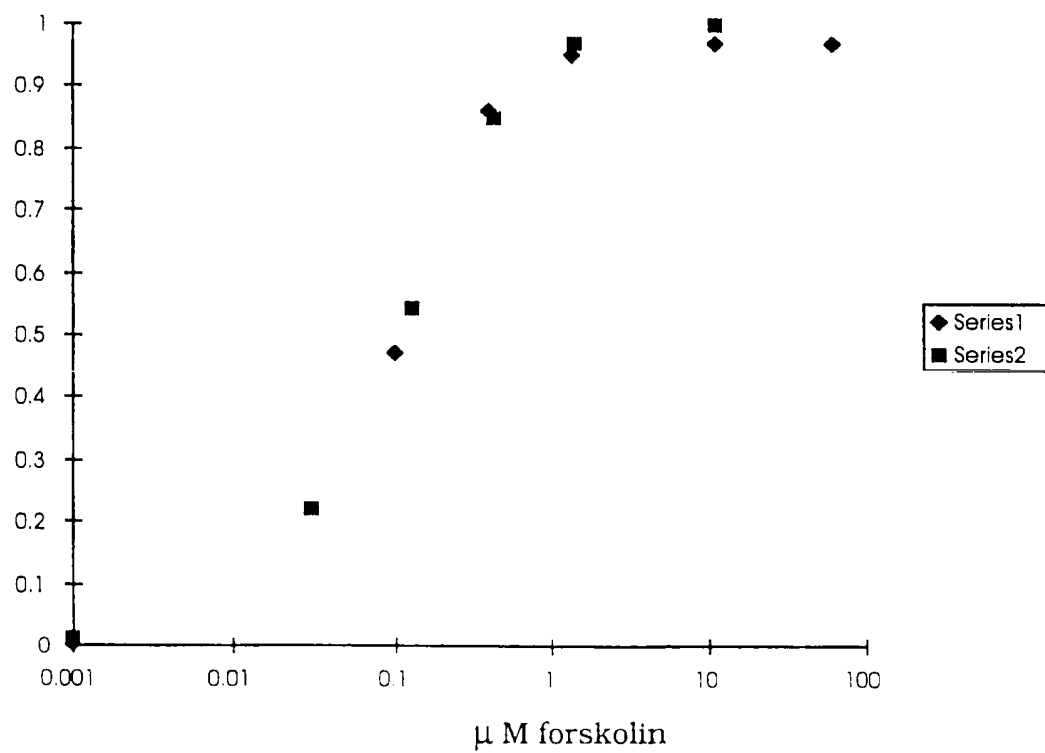
3/12

Fig 3



4/12

Fig 4



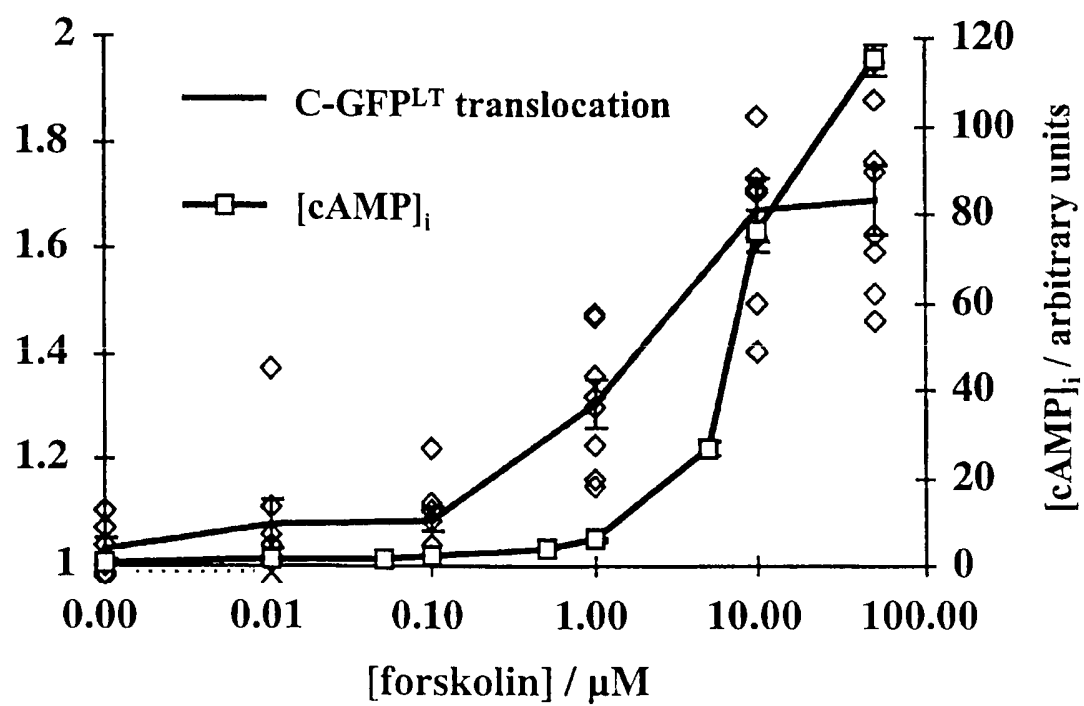
5 / 12

Fig 5

[forskolin] μ M	$t_{1/2\max}$ / s	t_{\max} / s
1	115 \pm 21	310 \pm 31
10	69 \pm 14	224 \pm 47
50	47 \pm 10	125 \pm 28

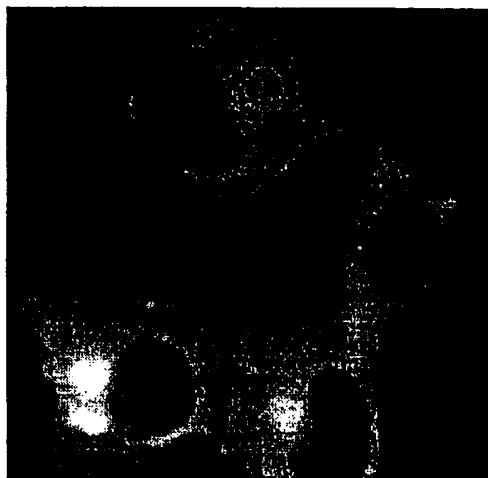
6/12

Fig 6

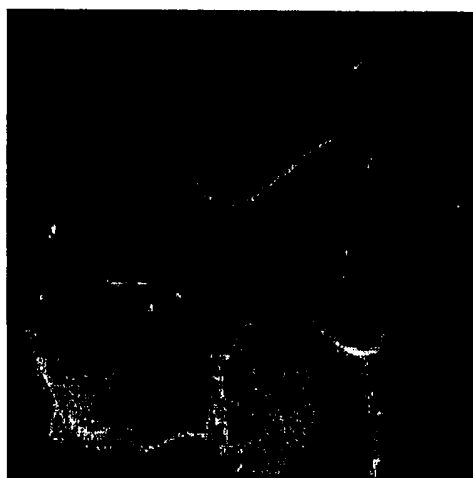


7 / 12

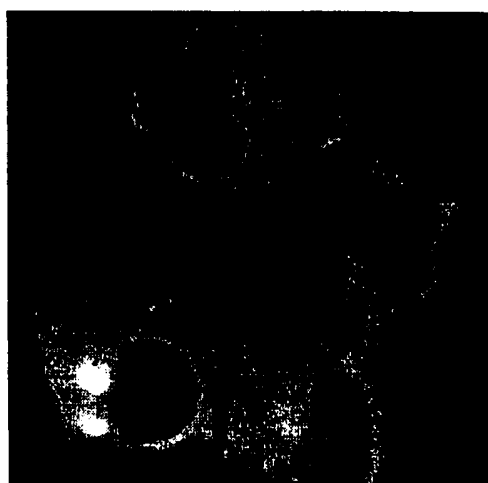
Fig 7



a)

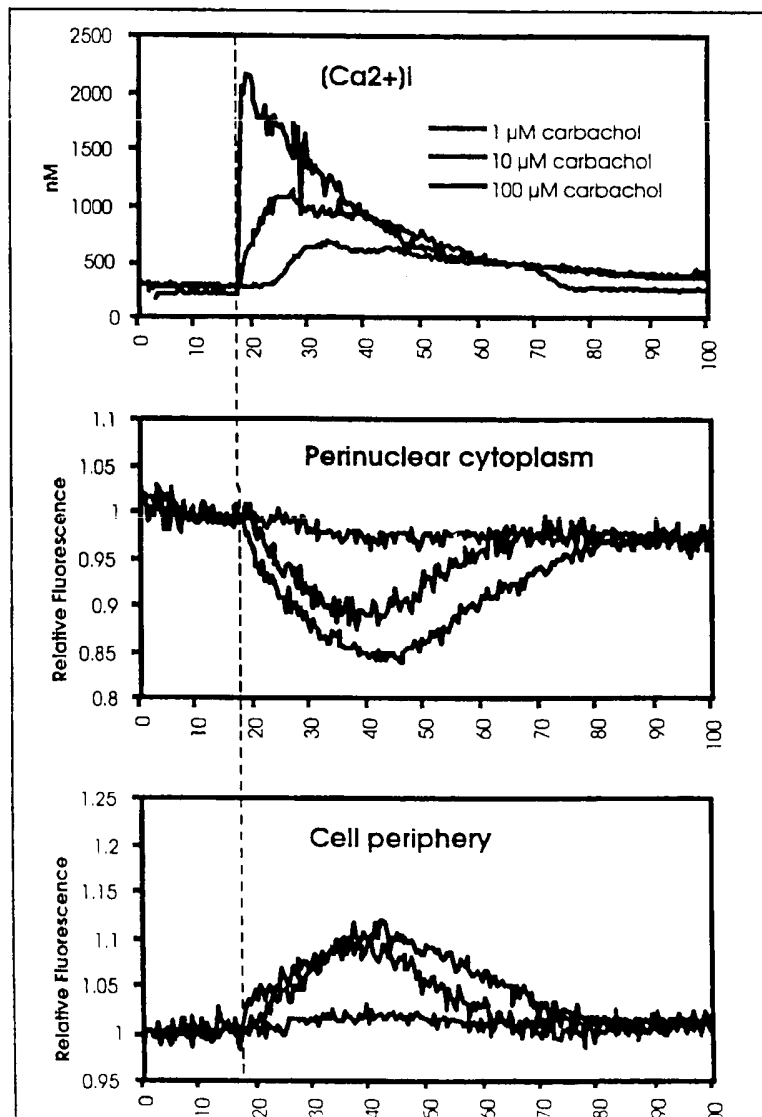


b)



8 / 12

Fig 8



9/12

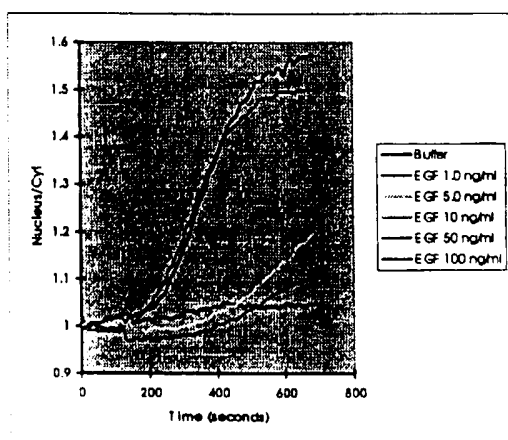
Fig 9



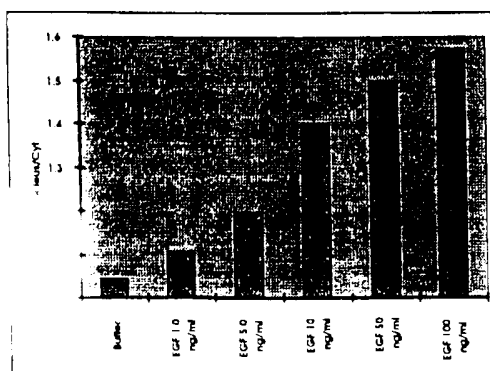
a)



b)



c)



d)

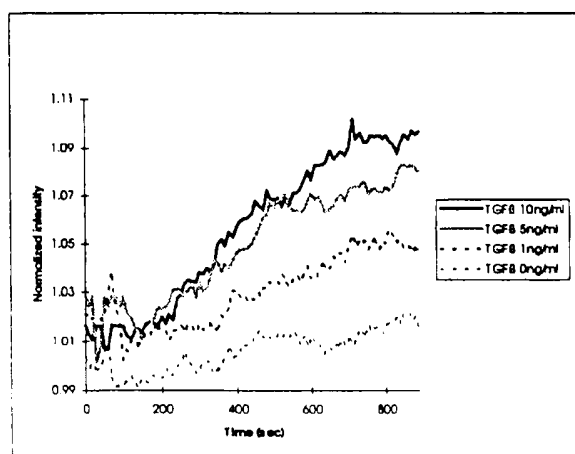
10 / 12

Fig 10

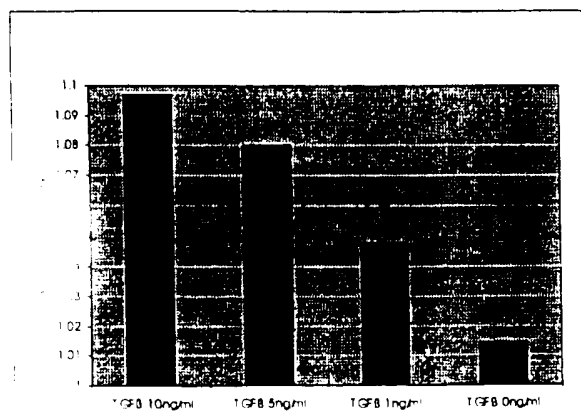
a)



b)



c)



11/12

Fig 11



12 / 12

Fig. 12

